

AD-A114 731

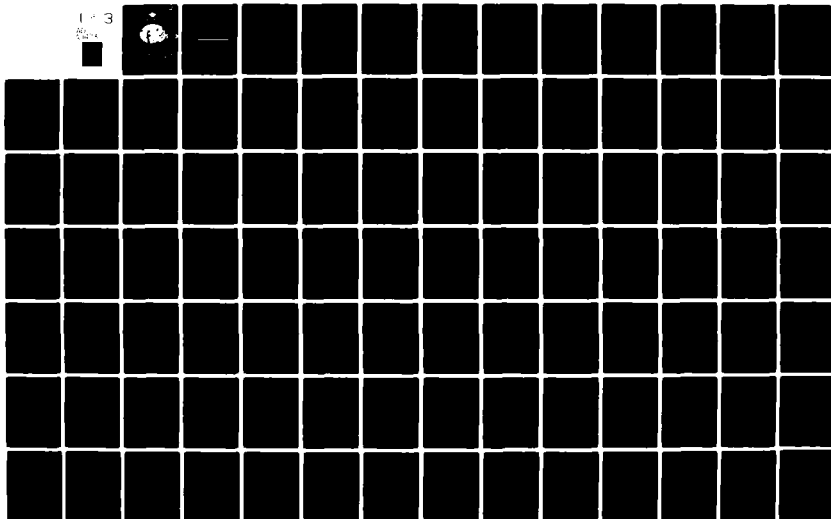
WILLIAM BEAUMONT ARMY MEDICAL CENTER EL PASO TX
ANNUAL PROGRESS REPORT, FISCAL YEAR 1981.(U)
SEP 81 L L PENNEY

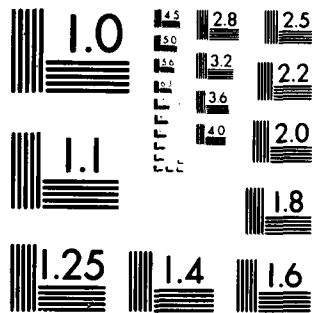
F/G 6/5

UNCLASSIFIED

NL

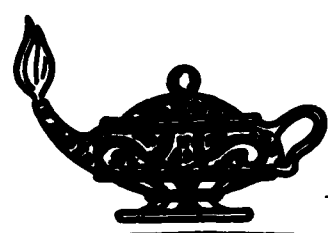
1-3





MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

12



WILLIAM BEAUMONT ARMY MEDICAL CENTER

WILLIAM



DTIC
ELECTE
MAY 20 1982
S D D

DEPT. OF CLINICAL INVESTIGATION

ANNUAL PROGRESS REPORT FISCAL YEAR 1981

THIS DOCUMENT HAS BEEN APPROVED FOR PUBLIC RELEASE:
ITS DISTRIBUTION IS UNLIMITED

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER #16	2. GOVT ACCESSION NO. AD-A114731	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Annual Progress Report FY81 William Beaumont Army Medical Center		5. TYPE OF REPORT & PERIOD COVERED Annual Progress Report (Final) 1 Oct 80 - 30 Sep 81
		6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) L.L. Penney, COL, MC		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS Department of Clinical Investigation William Beaumont Army Medical Center (ATZC-MDRD)		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS 3A062110A826))
11. CONTROLLING OFFICE NAME AND ADDRESS Human Use and Clinical Investigation Office SGRD-HR, Ft Detrick, Frederick MD 21701		12. REPORT DATE 30 September 1981
		13. NUMBER OF PAGES 231
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office) SGRD-HR, Ft Detrick, Frederick, MD 21701		15. SECURITY CLASS. (of this report) UNCLASSIFIED
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) This document has been approved for public circulation. Distribution is unlimited. [REDACTED]		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report) Same		
18. SUPPLEMENTARY NOTES		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) See Index		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) This report serves to detail the progress, status, and funding of approved projects conducted under protocol by staff members, interns, and residents at William Beaumont Army Medical Center. The varying projects as reported are classified according to the service or department to which the principal investigator belongs. Research conducted at WBAMC is categorized as either basic experimental medicine or trials and testing of clinical medicine procedures using the indigenous population for which this medical facility provides support.		

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

FOREWORD

The Department of Clinical Investigation, formerly Medical Research and Development, is entering its 17th year of operation. The long awaited goal of protocol activation following local approval for all protocols except IND studies was realized at the Commanding General's HSC Conference in May 1981.

Personnel shortages and uncertainty persisted, but further budgetary progress was realized in FY81. The Department is particularly indebted to BG Chester Ward, Commander, WBAMC, who has approved continued growth in our OMA funding, and who has authorized architectural design for an expansion to the existing Biological Research Facility. A portable building, which allows additional techniques and provides expanded capabilities in the animal model, was occupied in FY81.

The Department has fulfilled its mission in a productive manner. The investigators who actively pursued their projects, frequently utilizing their own hours from off-duty time, are to be especially commended. All investigators for each work unit are identified in the respective reporting sections.

The contributions of the many nurses, technicians, corpsmen and administrative personnel who are vital to the successful implementation of clinical research projects are appreciated. The committee members providing the critical review imperative in the proper conduct of our mission are acknowledged on the following page.

I am grateful for the editorial and typographical assistance of Ms Peggy Casteel in the completion of this document and to the remaining staff of the department for their varied areas of contribution. Mr. Shel Chaplain, ARC volunteer, has donated one day per week of general duties this year, and I thank him for his efforts.

L. L. Penney

L. L. PENNEY, M.D.
COL, MC
C, Dept Clinical Investigation

Accession For	
NTIS GRA&I	<input checked="" type="checkbox"/>
DTIC TAB	<input type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
A	



HUMAN USE COMMITTEE

COL Thomas Geer, MC
COL A. Kissack, MC
COL D. Boyce, MC
LTC R.R. Jungck, MSC
MAJ J.A. Szilvasy, CH
LTC W. York, MC
MAJ D.B. Craig, MC
CPT F.L. Melton, JAG
CPT M.L. Smith, MSC
Rev Hugh Goss

Chairman
C, Trauma Ctr
C, Family Planning
Social Work Service
Chaplain
C, Dept Pathology
C, Infectious Disease
JAG
Recorder
Non-Institutional member

CLINICAL INVESTIGATION COMMITTEE

COL Thomas Geer, MC
COL L.L. Penney, MC
COL J.T. Fay, DC
MAJ T.B. Jeffrey, MSC
CPT M.L. Smith, MSC
CPT A.W. O'Brien, VC

Chairman
C, Dept Clinical Investigation
C, Dental Research
Psychology Svc
Recorder
C, Biological Research Svc

ANIMAL USE COMMITTEE

COL L.L. Penney, MC
CPT W.J. Klenke, MSC
CPT A.W. O'Brien, VC

C, Dept Clinical Investigation
Nuclear Physicist
C, Biological Research Svc

RADIATION PROTECTION SUBCOMMITTEE

COL Thomas Geer, MC
COL L.L. Penney, MC
LTC R.M. Ball, MC
CPT S.G. Dunston, MSC

C, Professional Svc
C, Dept Clinical Investigation
C, Radiology
Recorder

TABLE OF CONTENTS

REPORT NO. 16	Page
Foreword.....	3
Table of Publications and Presentations FY81.....	16
Unit Summary Sheet.....	24
Details Sheets:	
<u>Department of Clinical Investigation</u>	
Work Unit No. 78/15 (FY78,0) Penicillin Alone vs Ampicillin and Gentamicin in the Treatment of Group B Streptococcal Sepsis.....	30
Work Unit No. 78/22 (FY78,C) The Efficacy of Active Immunization to Group B Streptococcal (GBS) Organisms in Preventing GBS Sepsis.....	32
Work Unit No. 79/01 (FY79,0) Role of Deoxyribonucleic Acid Attachment to Cell Membrane in the Regulation of Bacterial Growth.....	33
Work Unit No. 79/07 (FY79,0) Synthesis of Inhibitors of the Shikimate Pathway for Investigation as Potential Antimicrobial Agents.....	35
Work Unit No. 80/03 (FY80,0) Maternal Serum and Urinary Steroid Concentrations During Contraction Stress Testing.....	36
Work Unit No. 81/31 (FY81,0) Transfer of ¹³¹ I from Male to Female During Sexual Intercourse 37	
Work Unit No. 81/32 (FY81,0) Polyamines as Chemical Markers of the Response of Patients Being Treated for Cancer.....	38
Work Unit No. 81/33 (FY81,0) Study of the Size and Charge Heterogeneity of Prolactin in Human Seminal Plasma and Spermatozoa.....	39
Work Unit No. 81/34 (FY81,0) Location of Prolactin, HCG, LH, and FSH in Human Semen: An Immunocytochemical Study.....	41
Work Unit No. 81/46 (FY81,0) Inhibition of the Uterine Vascular Effects of 17 β Estradiol with the H ₂ Receptor Antagonist Cimetidine; Cortisol; an Adrenergic Blocking Agent, Phentolamine; and Cycloheximide.....	42

Work Unit No. 81/47 (FY81,0)
 Variability of Estradiol Induced Increases in Uterine Blood
 Flow as a Function of Time Post-oophorectomy..... 43

Work Unit No. 81/48 (FY81,0)
 Variability in Quantifiable Uterine Cytosolic and Nuclear
 Estrogen Receptors as a Function of Time Following
 Oophorectomy in Rabbits..... 44

Work Unit No. 81/53 (FY81,0)
 Prostacyclin Synthetic Capability of Thoraco-Abdominal Aortic
 Dacron Graft One Year Post-Surgery..... 45

Department of Dentistry

Work Unit No. 79/09 (FY79,C)
 Antibiotic Prophylaxis in Intraoral Orthognathic Surgery..... 46

Work Unit No. 80/29 (FY80,C)
 Serum Glucose Level in Relation to Recovery Time from General
 Anesthesia for Outpatient Oral Surgery Procedures..... 49

Work Unit No. 81/25 (FY81,0)
 A Clinical Comparison of Antibiotic Steroid Preparations Used in
 Post Extraction Mandibular Third Molar Sites to Reduce
 Associated Post-Operative Sequellae..... 50

Work Unit No. 81/26 (FY81,0)
 Use of Op Site Transparent and Permeable Adhesive Dressing in
 Skin Grafting..... 51

Department of Medicine

Work Unit No. 76/23 (FY76,T)
 Effect of a Broad Spectrum Antibiotic on the Course of Viral URI 53

Work Unit No. 76/33 (FY76,0)
 Diagnostic Adrenal Scanning with ¹³¹I (NP59)..... 54
 54

Work Unit No. 78/06 (FY78,T)
 Comparison of Cellular Metabolic Indices with Thyroid
 Dysfunction and Therapy..... 55

Work Unit No. 79/05 (FY79,C)
 Technetium 99m-Pyridoxylidoneglutamate (Tc-99m-PG) for Diagnosis
 of Hepatobiliary Disease..... 56

Work Unit No. 79/13 (FY79,T)
 Incidence of HL-A B27 Positivity in "Idiopathic" Aortic
 Insufficiency..... 58

Work Unit No. 79/14 (FY79,T) Clearing of Bacteria from Sputum of Patients with Chronic Bronchitis or Pneumonia Following Antibiotic Therapy.....	60
Work Unit No. 79/16 (FY79,T) Stage I and II Non-Hodgkins Lymphoma.....	61
Work Unit No. 79/21 (FY79,T) Adjuvant Melanoma.....	62
Work Unit No. 79/24 (FY79,T) Combined Modality for Recurrent Breast Cancer.....	63
Work Unit No. 79/26 (FY79,T) Treatment in Combination with BCNU, DTIC, or Procarbazine in Patients with Malignant Gliomas of the Brain.....	64
Work Unit No. 79/28 (FY79,O) Chemotherapy in Non-Hodgkins Lymphoma CHOP vs CHOP + Levamisole vs CHOP + Levamisole + BCG for Remission Induction Therapy.....	65
Work Unit No. 79/34 (FY79,O) Adjuvant Chemotherapy with 5-FU, Adriamycin and Metomycin C (FAM) vs Surgery Alone for Patients with Locally Advanced Gastric Adenocarcinoma Phase III.....	67
Work Unit No. 79/35 (FY79,O) Brain Metastases Phase III.....	68
Work Unit No. 79/36 (FY79,O) ROAP-ADOAP in Acute Leukemia, Phase III.....	69
Work Unit No. 80/1 (FY80,C) A Comparison of Development of Sensitivity to Penicillin in Normal and Atopic Individuals.....	70
Work Unit No. 80/8 (FY80,O) Evaluation of Thyroid Hormones in Alcoholic Hepatitis.....	71
Work Unit No. 80/10 (FY80,O) The Hematologic and Metabolic Status of Sick Cell Trait Individuals Following Vigorous Exercise.....	72
Work Unit No. 80/11 (FY80,O) Prospective Study of Mannitol in the Prevention of Radiographic Contrast Induced Acute Renal Failure.....	74
Work Unit No. 80/16 (FY80,O) An Investigation into the Effects of Cromolyn Sodium on Nonspecific Bronchial Hyperactivity.....	75

Work Unit No. 80/18 (FY80,0) Clinical Evaluation of Renal Cortical Imaging Utilizing 99mTc-Kidney Scintigraph.....	76
Work Unit No. 80/19 (FY80,0) Prevention of Gonadal Damage in Women Treated with Combination Chemotherapy or Radiotherapy Below the Diaphragm for Hodgkins or Non-Hodgkins Lymphoma.....	78
Work Unit No. 80/20 (FY80,0) Combined Modality Therapy for Breast Carcinoma, Phase III.....	79
Work Unit No. 80/21 (FY80,0) Chemotherapy for Multiple Myeloma Phase III.....	80
Work Unit No. 80/22 (FY80,0) Multimodal Therapy for Limited Small Cell Carcinomas of the Lung	81
Work Unit No. 80/23 (FY80,0) An Evaluation of Three Rapid Nonradioisotopic Methods for the Immune Complexes in Human Disease.....	82
Work Unit No. 80/24 (FY80,0) The Development of an Enzyme Linked Assay to Measure Human Allergen Specific Antibodies of the Immunoglobulins G and M Class.....	83
Work Unit No. 80/26 (FY80,0) Assessment of Hematologic and Neurologic Abnormalities in the Young Alcoholic Patient.....	84
Work Unit No. 80/28 (FY80,0) The Use of a New Multitest Applicator in the Evaluation of the Clinical Efficacy of Allergen Immunotherapy.....	85
Work Unit No. 80/31 (FY80,0) Direct and Indirect Radionuclide Cystography in the Detection of Vesicoureteral Reflux.....	86
Work Unit No. 80/32 (FY80,0) A Randomized Trial of Chemotherapy and Radiation Versus Radiation Alone in the Treatment of Advanced Non-small Cell Lung Cancer.....	87
Work Unit No. 80/33 (FY80,0) The Effect of Beta 2-Adrenergic Agents on Immunoglobulins.....	88
Work Unit No. 80/35 (FY80,0) Treatment of Early Squamous Cell Ca of the Head and Neck with Initial Surgery and/or Radiotherapy Followed by Chemotherapy vs No Further Treatment, Phase III.....	89

Work Unit No. 80/36 (FY80,0) Combined Modality Therapy with Chemotherapy, Radiotherapy and Surgery in Advanced Previously Untreated (Unresectable) Stage III and IV Epidermoid Cancer of the Head and Neck, Phase II....	90
Work Unit No. 80/37 (FY80,0) Combination Modality Treatment for Stage III and IV Hodgkins Disease MOPP No. 6, Phase III.....	91
Work Unit No. 80/38 (FY80,0) Radiation Therapy in Combination w/CCNU in Patients with Incompletely Resected Gliomas of the Brain Grade I and II	92
Work Unit No. 80/39 (FY80,0) Combined Modality Treatment for ER-Breast Cancer Phase III.....	93
Work Unit No. 80/40 (FY80,0) Exercise Induced Asthma in Basic Trainees.....	94
Work Unit No. 80/41 (FY80,0) Prevention of Gonadal Damage in Men Treated with Combination Chemotherapy/Radiotherapy for Hodgkins Disease and Non- Hodgkins Lymphomas.....	96
Work Unit No. 81/04 (FY81,0) Can Nuclear Scanning Predict Resolution of Osteomyelitis	97
Work Unit No. 81/05 (FY81,0) The Role of Food Allergy in the Pathogenesis of Migraine Headache.....	99
Work Unit No. 81/06 (FY81,T) Evaluation of Antidiar ^R and Lomotil ^R in Acute Diarrhea	101
Work Unit No. 81/08 (FY81,0) Effect of Simultaneous Streptokinase Reperfusion with Glk, Nifedipine, or Hyaluronidase on Infarct Size in the Canine Heart	102
Work Unit No. 81/09 (FY81,0) The Usefulness of Modern Clinical Immunologic Testing in the Prediction of Disease, a Pilot Study.....	105
Work Unit No. 81/10 (FY81,0) An Evaluation of the Effects of Beta II Adrenergic Agents on Human Immunoglobulins and Antibody Response.....	107
Work Unit No. 81/11 (FY81,0) Clinical Evaluation of Tc99m-PIPIDA-Tin as a Hepatobiliary Agent	109
Work Unit No. 81/12 (FY81,0) A Novel Method of Hyposensitization Therapy with Russian Thistle Antigen.....	111

Work Unit No. 81/13 (FY81,0) Effect of Streptokinase on the Sinoatrial Node, the Atrio-ventricular Node, and the Myocardium of the Canine Heart.....	113
Work Unit No. 81/15 (FY81,T) Treatment of Advanced Germ Cell Neoplasms of the Testis: Remission Induction with Vinblastine, Bleomycin with Low Dose or High Dose Cis-Platinum.....	114
Work Unit No. 81/16 (FY81,T) Chemoimmunotherapy in Stages III and IV Ovarian Carcinoma: A-C plus BCG, vs. A-C plus Cis-Platinum vs. A-C plus Cis-Platinum plus BCG, Phase III.....	115
Work Unit No. 81/17 (FY81,0) The Treatment of Chronic Stage CML with Pulse, Intermittent Busulfan Therapy with or without Oral Vitamin-A, Phase III.....	116
Work Unit No. 81/18 (FY81,0) Evaluation of Two Maintenance Regimens in the Treatment of Acute Lymphoblastic Leukemia in Adults, Phase III.....	117
Work Unit No. 81/19 (FY81,0) Preoperative Reductive Chemotherapy for Stage III or IV Operable Epidermoid Carcinoma of the Oral Cavity, Oropharynx, or Larynx..	118
Work Unit No. 81/20 (FY81,0) Colchicine in Refractory Chronic Lymphocytic Leukemia, Phase I-II	119
Work Unit No. 81/21 (FY81,0) Treatment for Advanced Adenocarcinoma and Large Cell Carcinoma of the Lung: FOMi vs CPA vs FOMi/CAP, Phase III.....	120
Work Unit NO. 81/22 (FY81,0) Evaluation of Two Combination Chemotherapy Programs, Adriamycin and Cis-Platinum (AP) versus Adriamycin, Cis-Platinum plus VP 16 (VAP), in the Treatment of Extensive Squamous Cell Carcinoma of the Lung, Phase III.....	121
Work Unit No. 81/23 (FY81,0) The Natural History of Pathological Stage T ₁₋₂ N ₀ M ₀ ER + Breast Cancer, Phase III.....	122
Work Unit No. 81/24 (FY81,0) The Re-Use of Hollow Fiber Hemodialyzer, a Randomized Trial....	123
Work Unit No. 81/28 (FY81,0) The Effects of Erythromycin Treatment on Neutrophil Chemotaxis.	124
Work Unit No. 81/29 (FY81,0) The Effect of a Lipoxigenase Inhibitor on Phytohemagglutinin Stimulated Lymphocyte Blastogenesis in Rheumatoid Arthritis....	126

Work Unit No. 81/30 (FY81,0) The Effect of a Histamine (H ₂) Antagonist on the Lupus-like Syndrome of New Zealand Mice.....	127
Work Unit No. 81/36 (FY81,0) Phase II Studies on Ketoconazole (KETO) - Comparison of Two Different Doses of Keto in Treating Coccidioidomycosis.....	128
Work Unit No. 81/38 (FY81,0) The Development of Subsensitvity to Atropine.....	129
Work Unit No. 81/39 (FY81,0) The Usefulness of NonAcetylated Salicylates in the Treatment of Inflammatory Disease in Patients with Aspirin Idiosyncratic Asthma.....	131
Work Unit No. 81/40 (FY81,0) The Usage of Beta 2 Agonist in Topical Treatment of Allergic Skin Reactions.....	133
Work Unit No. 81/45 (FY81,0) The Effects of Chronic Bronchoconstriction on Bronchial Smooth Muscle and Bronchial Architecture.....	134
Work Unit No. 81/54 (FY81,0) High Resolution Electrophoretic Screening of Body Fluid Proteins	136
Work Unit No. 81/56 (FY81,0) Ticlopidine Hydrochloride - A Clinical Trial in Patients with Transient Cerebral or Monocular Ischemic Attacks.....	138
Work Unit No. 81/57 (FY81,0) Late Incidence of Chronic and Occult Constrictive Pericardial Disease in Patients Treated by Radiotherapy for Hodgkins Disease	140
Work Unit No. 81/58 (FY81,0) The Prevalence of Antibiotic Tolerant Staphylococcus Aureus in Nasal Cultures of Different Adult Population Groups.....	141
Work Unit No. 81/64 (FY81,0) A Comparison of Streptokinase/Streptodornase (SK/SD) with Streptokinase (SK) alone in Delayed Hypersensitivity Skin Testing of Children Ages 5-17.....	143
Work Unit No. 81/65 (FY81,0) Utility of Furosemide in Early Oliguric Renal Failure.....	145
<u>Department of Nursing</u>	
Work Unit No. 81/27 (FY81,0) Effect of Reassessment on Deterioration of Diabetic Patients' Knowledge and Management Skills, and on Compliance.....	146

Work Unit No. 81/50 (FY81,C)	
Oxygenation and Subarachnoid Block Regional Anesthesia.....	147
Work Unit No. 81/51 (FY81,C)	
Preoperative Anxiety and Continuity of Anesthesia Care.....	149
Work Unit No. 81/52 (FY81,C)	
The Lawn Chair and Flat Positions and Their Relationship to Post-Operative Back Pain.....	151
Work Unit No. 81/60 (FY81,O)	
Hemolysis During Blood Administration.....	153
<u>Department of Obstetrics-Gynecology</u>	
Work Unit No. 74/01 (FY74,T)	
Umbilical Cord Lactate, Pyruvate, Betahydroxy Butyrate, pCO ₂ , pO ₂ , and pH Value in Normal and Abnormal Pregnancies.....	155
Work Unit No. 77/02 (FY77,O)	
Ultrastructural Investigation of Prostaglandins and Their Precursors in the Human Fetal Chorioamnionic Membrane.....	156
Work Unit No. 77/04 (FY77,C)	
Inhibition of Premature Labor with Terbutaline.....	157
Work Unit No. 77/06 (FY77,O)	
Study to Determine the Ability of Amniotic Fluid to Inhibit Growth of E. Coli.....	158
Work Unit No. 77/19 (FY77,C)	
The Effect of Prostaglandin Synthesis Inhibitors on Uterine Blood Flow.....	159
Work Unit No. 77/25 (FY77,O)	
A Comparison of Phospholipid Levels and Choline Phosphotrans- ferase (CPT) Activity in Amniotic Fluid and Newborn Tracheal Fluid.....	163
Work Unit No. 78/26 (FY78,C)	
Inhibition of the Vascular Effects of 17b Estradiol with Actinomycin D.....	164
Work Unit No. 79/04 (FY79,C)	
Prevention of Post-Cesarean Section Infections.....	166
Work Unit No. 80/09 (FY80,O)	
Effect of Terbutaline on Surface Active Phospholipids in Adult and Fetal Lung.....	168
Work Unit No. 80/17 (FY80,O)	
Transvaginal Absorption of Estrogens in Patients Following Pelvic Irradiation.....	169

Work Unit No. 80/25 (FY80,O) Placental Levels of 5a-dihydroprogesterone in Normal Pregnancy and Those Complicated by Pre-eclampsia.....	170
Work Unit No. 81/03 (FY81,O) Serial Measurement of Serum, Zinc, Magnesium, Copper, Lead, Lithium and Arsenic During Pregnancy.....	171
Work Unit No. 81/44 (FY81,O) Effect of Intravenous Terbutaline on Phospholipid Content of Adult Dog Lung.....	173
Work Unit No. 81/61 (FY81,O) Maternal and Fetal Effects of Verapamil, A Calcium Blocking Agent.....	174
<u>Department of Orthopedic Surgery</u>	
Work Unit No. 76/24 (FY76,O) An Investigation of the Effects of Supplemental Oxygen on Chemically Induced Fat Embolization.....	176
Work Unit No. 79/03 (FY79,O) Compartmental Pressure Studies as a Determinant for the Need for Fasciotomy.....	177
Work Unit No. 79/42 (FY79,O) The Incidence of Visual-Motor Perceptual Problems in Persons with Traumatic Hand Injuries.....	180
Work Unit No. 80/06 (FY80,C) Evaluation of Antagonistic Knee Flexors and Extensors During Prone and Supine Resistive Exercise Using Electromyography.....	182
<u>Department of Pathology</u>	
Work Unit No. 70/111 (FY70,C) Molecular Etching.....	184
<u>Department of Pediatrics</u>	
Work Unit No. 77/10 (FY77,O) Zinc Levels in Maternal Infant Pairs.....	185
Work Unit No. 77/13 (FY77,O) Investigation of the Effects of Diphenylhydantoin on Intellectual Functioning of Children.....	186
Work Unit No. 78/14 (FY78,C) Maintenance of Patency of the Ductus Arteriosus in Congenital Cardiac Lesion.....	187

Work Unit No. 78/25 (FY78,0)	
Antibiotic Prophylaxis for Recurrent Otitis Media: Comparison of Sulfasoxizole, Erythromycin, and Placebo.....	188
Work Unit No. 80/02 (FY80,0)	
Developmental Analysis of Heavy and Trace Element Hair Content in Normal Children and Children with Attention Disorders.....	189
Work Unit No. 80/27 (FY80,C)	
Investigation of the Concerns, Perceptions and Expectations of Parents Coming to the Developmental Evaluation Clinic for the First Time.....	191
Work Unit No. 80/34 (FY80,0)	
Counterimmunoelectrophoresis in Nonsuppurative Otitis Media....	193
Work Unit No. 81/42 (FY81,0)	
The Recognition and Frequency of the Polycystic Ovary Syndrome in a General Adolescent Population.....	194
Work Unit No. 81/59 (FY81,0)	
A Longitudinal Prospective Study of the Neurological and Electrophysiologic Development of the Postmature Child.....	195
Work Unit No. 81/62 (FY81,0)	
Treatment of Middle Ear Effusions with Oral Hydrocortisone Versus Placebo.....	197
Work Unit No. 81/66 (FY81,0)	
Single Day Therapy with Trimethoprim-Sulfamethoxalate for Lower Urinary Tract Infection in Children.....	199
<u>Department of Psychiatry</u>	
Work Unit No. 81/37 (FY81,0)	
Torque and Its Relationship to Academic Achievement and Behavior in Children.....	201
<u>Department of Surgery</u>	
Work Unit No. 76/09 (FY76,T)	
Development of a Computerized Trauma Registry.....	203
Work Unit No. 78/03 (FY78,0)	
National Intraocular Lens Implantation Study.....	204
Work Unit No. 79/43 (FY79,T)	
Perioperative Thrombosis Prophylaxis in Patients with Peripheral Vascular Disease.....	205
Work Unit No. 80/12(FY80,0)	
Effect of Systemic Anti-Neoplastic Chemotherapy on Dacron Graft Incorporation.....	208

Work Unit No. 80/30 (FY80,T) Physiologic Monitoring and the Manipulation in the Aortic Reconstruction Patient.....	216
Work Unit No. 80/42 (FY80,T) Pilot Study for the Use of the Automated Autologous Blood Recovery System (Cell Saver) in Blunt and Penetrating Abdominal Trauma.....	217
Work Unit No. 81/02 (FY81,0) Replacement of the Infra-Renal Inferior Vena Cava with an Improved Expanded Polyfluorotetraethylene (e-PTFE) Graft and Comparison of Two Grafts.....	219
Work Unit 81/07 (FY81,0) Comparison of Mortality and Morbidity of Uretero- ileocecosigmoidostomy with Other Urinary Diversions.....	221
Work Unit 81/49 (FY81,T) A Comparison of Techniques for Obtaining Tissue for Estrogen Receptor Analysis in Human Breast Cancer.....	223
Author Index.....	224
Keyword Index.....	227

DEPARTMENT OF CLINICAL INVESTIGATION

Benedetto, AR, Klenke WJ: Theoretical and Applied Techniques in Gamma Camera Uniformity Quality Control. Presented at the Southwestern Chapter, Society of Nuclear Medicine, 29 Mar 81.(C)

Frederick, RJ: Rifampicin Refractory RNA Synthesis in a Sensitive E. coli Strain Infected with Bacteriophage T4. Submitted for publication.(C)

Frederick, RJ: Immunological Protection of Adult Rabbits Against Early-Onset Like Group B Streptococcal Sepsis. Submitted to J Infect Dis.(C)

Rauls D, Penney LL: Analysis of Olivetol in Rabbit Serum. Submitted to the J Chromatography(C)

Daniell W, Rauls D, Penney LL: The Effect of Terbutaline on the Phospholipid Composition of Beagle Dog Tracheal Wash. Submitted to the Amer Rev Resp Dis (C)

Penney LL, Daniell WC: Estimation of Success in Treatment of Premature Labor: Applicability of Prolongation Index in a Double-Blind, Controlled, Randomized Trial. Am J Obstet Gynecol 138:345, 1980(C).

Penney LL: Ratio of Unconjugated to Total Estriol in Uncomplicated Third-Trimester Pregnancy. J Reprod Med 25:259, 1981(C).

Penney LL: Estimation of Gestational Age and Maternal Serum Steroid Concentrations. Unconjugated Estriol. J Steroid Biochem 13:1443, 1981(C).

Penney LL, Klenke WJ: Variability in Unconjugated and Total Estriol in Serum During Normal Third Trimester Pregnancy. Clin Chem 26:1811, 1981(C).

Penney LL: Estimation of Gestational Age and Maternal Serum Steroid Concentrations: Total Estriol. Am J Obstet Gynecol 138:745, 1981(C).

Penney LL, Ruangwit UI, Miles PA: Congenital Lipodystrophy and Polycystic Ovarian Disease. J Reprod Med 26:145, 1981.

Penney LL, Killam AP: Amniotic Fluid Cortisol and Maternal Serum Cortisol. (Ltr to Editor) Acta Obstet Gynecol Scand. In press(C).

Betz G., Engel T., Penney LL: Tuboplasty - Comparison of the Methodology. Fertil and Steril 34:534, 1981.

Plymate SR, Fariss BL, Smith ML, Jacob WH, Matej LA: Seminal Fluid Androgen Binding Protein. Andrologia 13:308, 1981 (C,MAMC).

DEPARTMENT OF MEDICINE

Billingsley JL, Redwine MD, Lundy MM, Daniels DL: Combined Bone and Gallium Scanning for the Diagnosis of Osteomyelitis. Scientific Exhibit at the 28th Annual Meeting of the Society of Nuclear Medicine, Las Vegas, 1981.

Brown JM, McAuley RJ, Lull RJ, Bunker SR, Sobol SM: Amyloid Cardiomyopathy: Diagnosis by Tc-99m Pyrophosphate (PYP) and Tc-99m Hydroxymethylene Diphosphate (HMDP) Scintigraphy, but not by Tc-99m Methylene Diphosphate (MDP) Scintigraphy. Presented at the Sixth Annual Western Regional Meeting, Society of Nuclear Medicine, San Francisco, 1981.

Brown JM, White CJ, Sobol SM, Lull RJ: Increased Left Ventricular Ejection Fraction After a Meal: Potential Source of Error in Performance of Radionuclide Angiography. Presented at the Sixth Annual Western Regional Meeting, Society of Nuclear Medicine, San Francisco, 1981.

Daniels DL, Henry HW: Graphic Presentation of Blood Volume Findings. Scientific Exhibit at the 28th Annual Meeting of the Society of Nuclear Medicine, Las Vegas, 1981.

Daniels DL, Henry HW: Selective Performance of the T₃ Uptake: A Practical Approach to Thyroid Function Studies. Concise Communication. J Nucl Med 22:606, 1981.

Hoadley S: Nocardiosis. Presented at Advances in Internal Medicine Seminar, Letterman Army Medical Center, Oct 1980.

Maccario M: Developmental Dysphasia and EEG. Dev Med and Child Neurol, in press.

Mansfield LE, Nelson HS: Allergens in Commercial Housedust. Accepted for publication in Annals of Allergy.

Mansfield LE, Hameister HH, Spaulding HS, Smith NJ, Glab N: The Role of the Vagus Nerve in Airway Narrowing Caused by Intraesophageal Hydrochloric Acid Provocation and Esophageal Distention. Accepted for publication in Annals of Allergy.

Mansfield LE, Nelson HS: The Effect of Beta Adrenergic Agents on Immunoglobulin-G Levels in Asthmatic Subjects: Accepted for publication in Intern Arch Allergy Appl Immunol (C, WBAMC and FAMC).

Mansfield LE: Systemic Reactions to a Natural Health Food Used to Treat Seasonal Allergic Rhinitis. Presented at the American College of Allergists 37th Annual Congress in Washington D.C. April 1981.

Mansfield LE: The Effects of Beta Adrenergic Agents and Prednisone on Serum Immunoglobulins and Complement Levels of Asthmatic Patients. Presented at the American College of Allergists 37th Annual Congress in Washington, D.C. April 1981.

Mansfield LE, Goldstein GB: Anaphylactic Reaction After Ingestion of Local Bee Pollen. *Annals of Allergy*

Moreno AL, Spicer MG, Old C, Morrison RE: Varicella Pneumonia in Pregnancy with Lactate Production and Marantic Endocarditis. Submitted for publication.

Morrison RE, Rychly R, Pitcher JL: Development of Meningitis During Penicillin Therapy for *S. Pneumoniae* Pneumonia. Submitted to *Military Medicine*.

Morrison RE, Brown J, Waters T, Spicer M: Myocarditis and Adult RDS Caused by *Toxoplasma Gondii* in a Previously Healthy Adult. Accepted for publication in *Current Topics in Internal Medicine*.

Nusynowitz ML, Sonnemaker RE, Floyd JL: Selection of Patients for Coronary Arteriography with Thallium-201: Operating Position on the Receiver Operating Characteristic Curve. *Int J Nucl Med & Biol* 8:204, 1981(C).

Old CW, Duarte CG, Siedlecki M: Effects of DOCA in K-Depleted Rats. *Kidney International*, Vol 19, 1981.

Old CW: Effect of Mannitol in the Prevention of Radiocontrast Acute Renal Failure. *Clin Res* 29:427, 1981(C).

Old CW: Mannitol in the Prevention of Radiocontrast Acute Renal Failure. Presented at the Kimbrough Urological Seminar, San Diego, (C).

Old CW, Duarte CG: Effect of DOCA on Plasma Volume in K-Depleted Rats. *Fed Proc* 40:554, 1981.

Old CW, Nickles D: Lipedema, Two Unusual Cases. Submitted to *JAMA*.

Parker AL, Knight J, Morrison RE: *Pseudomonas aeruginosa*, Botryomycosis of the Sternum. Submitted for publication.

Stein MR, Towner TG, Weber RW, Mansfield LE, Jacobson KW, McDonnell JT, Nelson HS: The Effect of Theophylline on the Lower Esophageal Sphincter Pressure. *Ann Allergy* 45:238, 1980.

Ting S, Zweiman B, Lavker R. Effects of Local Terbutaline on Histamine, Cellular Inflammatory Response and Ultramicroscopic Mast Cell Changes in Antigen Challenged Skin Sites in 5 Ragweed Sensitive Volunteers. Presented at the Annual Meeting of the American Academy of Allergy, San Francisco, March 1981.

Turnbull GL, Brown TJ, Rauls D, Collins J, Henry HW, Parker G, Daniels D: Effect of Systemic Anti-Neoplastic Chemotherapy on Dacron Graft Incorporation. Scientific Exhibit at the 28th Annual Meeting of the Society of Nuclear Medicine, Las Vegas, Jun 1981(C).

DEPARTMENT OF NURSING

Pesetski JD: A Practical Guide for Perioperative Practice. Assoc Oper Rm Nurs J, Dec 1980.

Thompson DA: Cardiovascular Assessment: Guide for Nurses and Other Health Professionals. Book published by the C.V. Mosby Company, 1981.

Thompson DA: Anticoagulant Client Education. Accepted for publication in the Amer J Nursing.

DEPARTMENT OF OBSTETRICS AND GYNECOLOGY:

Daniell WC, Penney LL, Reimann BEF, Parker GW, Rauls DO. Inhibitory Effects of Δ^9 -Tetrahydrocannabinol on Uterine and Placental Perfusion in Rabbits. IRCS Med Sci 9:947, 1981(C)

Howard TE, Daniell WC, Penney LL, Killam AP: A Double Blind Randomized Study of Terbutaline in Premature Labor. Presented at the Armed Forces District Meeting, American College of Obstet Gynecol, Orlando, Fla, October 1980(C).

Howard TE, Penney LL, Killam AP, Daniell WC. A Double Blind Randomized Study of Terbutaline in Premature Labor. Military Medicine, in press (C).

Reamy K: Treatment of Vaginismus by the Gynecologist: An Eclectic Approach. Accepted for publication in Obstet Gynecol.

Stafford JO, Daniell WC, Penney LL, Killam AP: Rhogam Monitoring. Fetaldex Versus Detection of Circulating Anti-Rho(D). Presented at the Armed Forces District Meeting, American College of Obstet Gynecol, Orlando, Fla, October 1980(C).

Reamy K: Sexuality and Pregnancy: A Review Accepted for publication in Arch Sex Behav.

White SE, Levine ES, Reamy K: Psychological Aspects of Sexuality During Pregnancy. Presented at the New Mexico State University College of Education Dialogue Series, Apr 21, 1981.

DEPARTMENT OF ORTHOPAEDIC SURGERY

Copeland R: Tendon Transfers: Motor Power or Confusion. Presented at the 44th Annual Meeting, Western Orthopaedic Association, Honolulu, Hawaii 18 Oct 1980.

Covarrubias GA, Kureshi ZU: Sagital Amputations: The Beaumont Experience. Presented at the Society of Military Orthopaedic Surgeons Meeting, Wilford Hall, San Antonio, TX 2 Nov 1980.

Hopkins CD: Talar Coalitions. Presented at the Society of Military Orthopaedic Surgeons Meeting, Wilford Hall, San Antonio, TX, 2 Nov 1980.

Huntt HA: Fractures of the Carpal Scaphoid in Children. Presented at the Carrie Tingley Hospital and New Mexico Chapter, Western Orthopaedic Association, Winter Orthopaedic Seminar, 12 Dec 1980.

Scully TJ: Stress Fractures: The Fort Bliss Success Story. Presented at the Society of Military Orthopaedic Surgeons Meeting, Wilford Hall, San Antonio, TX, 2 Nov 1980(C).

Scully TJ: Kinematic Analysis of Total Knee Joint Replacement. Presented at the Society of Military Orthopaedic Surgeons Meeting, Wilford Hall, San Antonio, TX, 2 Nov 1980.

Scully TJ, Besterman G: Stress Fracture - A Preventable Training Injury: Accepted for publication in Military Medicine(C).

Smith WR, Lee SH, Vichick DA: Evaluation of Antagonistic Knee Flexors and Extensors in the Prone and Supine. Presented at the Society of Military Orthopaedic Surgeons Meeting, Wilford Hall, San Antonio, TX, 2 Nov 1980(C).

Vichick DA. Care and Management of Combat Wounds. Presented at the University of Oklahoma, March 1981.

DEPARTMENT OF PATHOLOGY

Friedman HL: Are Chronic Exposure to Microwaves and Polycythemia Associated? Ltr to Editor New Engl J Med 304:357, 1981

Herrera GA, Reimann BEF, Scully TJ, DeFiore RJ: Non-ossifying Fibroma: Electron Microscopic Examination of a Case Supporting a Histiocytic Rather than a Fibroblastic Origin. Presented at the Society of Military Orthopedic Surgeons, San Antonio, Tex, 2 Nov 1980.

Herrera GA, Reimann BEF: The Use of Electron Microscopy in Adenocarcinomas of Unknown Origin. Presented at the Armed Forces Society of Laboratory Scientists, Arlington, VA, 12 Nov 1980.

Herrera GA, Mendoza A. Primary Canine Cutaneous Meningioma. Veterinary Pathology 18:127, 1981.

Cerezo L, Herrera GA. Clear Nuclei in Hemangioblastoma, Case Report and Ultrastructural Study. Arch Pathol Lab Med 105:331, 1981.

Herrera GA: The Use of Electron Microscopy in Adenocarcinomas of Unknown Origin (Abst) Proceedings 10:15, 1981.

Herrera GA, Head D: Histiocytic Lymphoma Arising at the Site of ALG Injection. Military Medicine 146:652, 1981.

Gomez A, Herrera GA, Kern S. Malignant Schwannoma with Rhabdomyoblastic Differentiation Arising on a Long-Standing Osteomyelitis. Accepted for publication in Cancer.

Chaffin J, Herrera GA, Roberts Ch. Oat Cell Carcinoma of the Trachea: A Case Report with Electron Microscopy. Accepted for publication in Ultrastructural Pathology.

Herrera GA, Reimann BEF, Scully T, DiFiore RJ: Non-Ossifying Fibroma: Electron Microscopic Examination of two cases Supporting a Histiocytic Rather than a Fibroblastic Origin. Accepted for publication in Clin Orth Rel Res.

Herrera GA, Reimann BEF, Salwas J, Turbat E: Malignant Schwannomas Presenting as Malignant Fibrous Histiocytomas. Accepted for publication in Ultrastructural Pathology.

Mead JH, Herrera GA, Kaufman MF, Herz JH: Case Report of a Primary Cystic Sarcoma of the Kidney Demonstrating Fibrohistiocytic, Osteoid and Cartilaginous Components, (Malignant Mesenchymoma). Accepted for publication in Cancer.

Reimann BEF: The Establishment of the New Electron Microscopy Lab in the Hospital. Presented at the Meeting of the Society of Armed Forces Medical Laboratory Scientists, Wash DC Nov 1980.

DEPARTMENT OF PEDIATRICS

Butler A: Rubella Susceptibility in an Adolescent Population. Pediatric Research 15:440, 1981(C).

Heath RE, Rogers JA, Cheldelin LV, Killam AP: Streptococcus Sanguis Sepsis and Meningitis: A Complication of Vacuum Extraction. Amer J Obstet Gynecol 138:343, 1980.

Lampe RM, Weir MR, McLeod H, Aspinall K, Artalejo L: Tympanometry in Acute Otitis Media. Am J Dis Child 135:233, 1981(C).

Lampe RM, McLeod HL, Weir MR, Artalejo L: A Clinical Trial of Antihistamine, Decongestant, or Placebo in Antibiotic-Treated Acute Otitis Media Followed with Pneumatic Otoscopy and Impedance Tympanometry. Military Medicine 146:259, 1981(C).

Lorenzen E, Schydlower M, Butler A, LaForce W, Schwab J, Shervette R, Swaney J: Adolescent Male Genital Disorders. Presented at the Uniformed Services Academy of Family Practice Scientific Convention, Memphis, Tenn, Apr 81.

Patterson S, Burg K: Care of the Child with Reyes Syndrome. Presented at the Symposium on Care of the Critically Ill Pediatric Patient, Texas Tech University Regional Academic Health Center, El Paso, TX 27 Jun 1981.

Schydlower M, Butler A, LaForce W, Lorenzen E, Schwab J, Shervette R, Swaney J. Exhibit, Uniformed Services Academy of Family Practice Scientific Convention 25 Apr 81 Memphis Tn.

Schydlower M: Breast Masses in Adolescents. Accepted for publication in Amer Family Physician.

Schydlower M, Greenberg H, Patterson P: Adolescents with Abnormal Cervical Cytology. Accepted for publication in Clinical Pediatrics

Weir MR: Natriuretic Hyponatremic Seizures in Infancy: The Case for SIADH. Case Reports. Military Medicine 145:851,1980.

Lampe RM, Copeland RL, Morrison RE: Soft Tissue Infection Associated with Haemophilus-Aphrophilus. Pediatrics 67:430, 1981.

White C: Resuscitation of the Pediatric Patient. Presented at the Symposium on Care of the Critically Ill Pediatric Patient, Texas Tech University Regional Academic Health Center, El Paso, TX 27 Jun 1981.

DEPARTMENT OF SURGERY

Cavanaugh DG, Youkey JR, Geer TM: Pulmonary Resection in Children: Case Report. Military Medicine 145:819, 1980.

Livaudais W, Cavanaugh DG, Geer TM: Rapid Postoperative Thoracotomy for Torsion of the Left Lower Lobe. Military Medicine, October 1980.

PREVENTIVE MEDICINE ACTIVITY

Gauld JR: Conjunctivitis Caused by Unshielded Mercury-Vapor Lamps. Submitted for publication.

Silsby HD, Gauld JR, Ramirez G: Cockpit Heat Stress in the AH-IG "Huey Cobra" Helicopter While Flying Nap-of-the-Earth. Aviation Digest, January 1981.

VETERINARY ACTIVITY

Couvillion CE, Jenney EW, Pearson JE, Coker ME: Survey for Antibodies to Bovine Virus Diarrhea, Bluetongue Virus and Epizootic Hemorrhagic Disease Virus in Mule Deer in Southern New Mexico. J Amer Vet Assoc Vol 177, Nov 1980.

UNIT SUMMARY

OBJECTIVES

The Department of Clinical Investigation, William Beaumont Army Medical Center, was established 2 February 1965 as the Medical Research and Development Service. The mission is to promote and coordinate clinical research and directed basic research. The policies and objectives are outlined in Department of Defense Directive Number 6000.4 dated 7 April 1971:

"Clinical investigation is an essential component of optimum medical care and consists of the organized inquiry into clinical health problems, for the following purposes:

1. To achieve continuous improvement in the quality of patient care.
2. To provide experience in the mental discipline achieved by participation in such organized inquiries, and to provide experience for personnel who will ultimately be teaching chiefs in military hospitals and medical specialty consultants.
3. To maintain an atmosphere of inquiry because of the dynamic nature of the health sciences.
4. To maintain high professional standing and accreditation of advanced health education programs."

Item number 4 has become especially critical in the wake of the GMENAC recommendations and the move to eliminate training programs. WBAMC is particularly vulnerable as this institution is essentially free-standing and has for several years suffered absolute and relative physician and allied scientist understaffing.

The Department supports in-house research projects by AMEDD staff members, residents, and interns, assisting in the formulation, preparation, and promulgation of research protocols and final research publications. The Department furnishes experimental design and statistical and technical expertise, develops and carries out special laboratory procedures, and provides general support in terms of equipment, supplies, and animal resources when necessary. Through contractual services in FY81 the department has provided enhanced statistical support at the PhD level, to investigators at

WBAMC. The creative and inspirational environment and technical knowledge available serve to stimulate the undertaking of basic and clinical medical and paramedical research at William Beaumont Army Medical Center by staff members, and interns and residents in training, as well as provide a basic instructional facility to elucidate the principles and conduct of research.

In addition to the primary mission, as stated above, the department is active in supporting several training and teaching programs involved with direct patient care. For example, the Biological Research Service directly supports approximately 450 anesthesia and surgical assistance training procedures annually ranging from minor suturing techniques for the Clinical Specialist Course students through aortic bypass grafts for the surgical residents. Examples of formal training protocols supported by the department were detailed in FY80 and are available upon request.

The Department of Clinical Investigation has provided scientific and administrative computational support to the Departments of Nursing, Pathology, Medicine, Surgery, and Logistics Division of WBAMC. The department provides this support as it alone possesses unique skills and equipment necessary to perform the tasks. The tasks may require mathematical modeling, statistical analysis, or graphical representations.

In addition, all radioimmunoassay calculations and reports performed by Nuclear Medicine were done utilizing equipments and programs provided by the Department of Clinical Investigation.

TECHNICAL APPROACH

The Department of Clinical Investigation provides support for staff research projects under the guidelines of the Declaration of Helsinki, Clinical Investigation Program (AR 40-38), HSC Reg 40-2, and the Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances (AR 40-7). Research is conducted under protocols approved by the Research Committee (WBAMC HR 70-4), the Human Use Committee (WBAMC HR 40-38) and the Radioisotope Committee (WBAMC HR 40-37) where applicable. In those research protocols utilizing laboratory animals, the investigators follow guidelines set forth in "Guide for Laboratory Animal Facilities and Care," published by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences-National Research Council, and the criteria established by the American Association for Accreditation of Laboratory Animal Care.

MANPOWER

<u>Title</u>	<u>Recognized Requirement (SSI/MOS)</u>	<u>Auth</u>	<u>Assigned</u>	<u>Name</u>
Chief	60 J00	0-5	0-6	Penney, L.L.
Biochemist/ Office of Chief	68 C00	0-3	0-3	Smith, M.L.
Biochemist/ Chem Svc	68 C00	0-3	-	--
Immunologist/ Microb Svc	68 E00	-	0-3	Serio, C.S.
Vet Lab Anm Off	64 C	0-3	0-3	O'Brien, A.W.
Med Lab NCO	92 B30	-	-	--
Biochem Sci Asst	01H20	E-5	E-7	Robinson, B.H.
Vet Anm Sp	91T20	E-5	E-5	Clark, G.L.
Biochem Sci Ass	01H20	-	E-5	Morales, J.A.
Vet Anm Sp	91T20	-	-	--
Vet Anm Sp	91T10	E-4	E-4	Flores, L.L.
Vet Anm Sp	91T10	E-3	E-3	Jamison, J.J.
Vet Anm Sp	91T10	E-3	-	--
Hlth Tech/ Anm Res Asst	00699	GS-7	GS-7	Revels, J.E.
Anm Caretaker	07706	WG-3	WG-1	Burton, A.D.
Chemist	01311	GS-12	GS-12	Rauls, D.O.
Microbiologist	00403	GS-12	GS-12	Frederick, R.J.
Chemist	01320	GS-9	GS-9	Sandison, S.W.
Immunochemist	01320	GS-9	GS-9	Meyers, T.T.
Med Lab Tech	00645	GS-7	GS-7	Manna, B.S.
Med Lab Tech	00645	GS-7	GS-6	Crouch, S.K.
Med Lab Tech	00645	-	-	--
Med Lab Tech	00645	-	-	--
Electron Micr Tech	00699	-	-	--
Med Lab Aide	00645	-	-	--
Editorial Asst	01087	GS-7	GS-7	Casteel, P.J.
Clerk Typist	00322	-	-	--

This manpower listing reflects the reorganization of the Laboratory Section into a Chemistry Svc and a Microbiology Svc. It also reflects approval of seven new recognized requirements from an interim Schedule X. Note that the DCI is operating at 67 % of recognized requirements. It should also be noted that the entire military contingent in the Biological Research Svc was reassigned in FY81. Lack of effective research for about four months resulted from the hiatus created. Additional allocations against the newly recognized requirements will be critical.

EXPENDITURES	FY78	FY79	FY80	FY81
Personnel (Civilian)	118,995	151,769	171,444	198,298
Consumable Supplies	35,923	34,392	60,134	86,351
MEDCASE Equipment	33,169	37,333	140,868	203,884*
Capital Equipment	-	2,425	10,427	36,256
TDY	2,805	1,179	1,469	2,387
Contracts, Services, Printing & Reproduction	3,053	937	1,025	3,518
TOTAL	\$193,945--	\$228,035-	388,835-	530,694-
Military Pay		141,385	167,437	217,503
		\$369,420-	\$556,272	\$748,197

*The MEDCASE expenditure includes a year-end supplement of \$85,000 for a cell sorter. The Dept Clinical Investigation further accounted the supply expenditures into general office \$3,596; general laboratory (divided among two or more protocols or for maintenance, standards, etc) \$24,704; and general biologic research facility (primarily training protocols) \$8,086. The remaining \$49,965 was spent on 36 specific protocols and the amount is noted under OMA cost on the appropriate detail sheets. The figures are annual for FY81, and, in parentheses, accumulative. Major equipment purchased specifically for a given protocol is accounted under MEDCASE for that protocol. Most equipment is for diverse uses and cannot be accounted on individual protocols.

It is impossible to account equipment, personnel, TDY and general supplies to specific protocols. However eliminating terminated protocols, there were 116 active protocols in FY81. The following figures will be high estimates because a portion of personnel, supply, and equipment expense is for training as opposed to research. Furthermore, all of the salary for the C, Dept Clinical Investigation is accounted here and a portion of his time is actually spent in patient care and teaching.

Comptroller data listing of \$748,197, indicates an overall average of \$6,450 total expenditure per active protocol. Several of the older protocols received more limited funding in deference to those more current. It is also important to note that a large clinical study, with little or no equipment or laboratory expense, can be quite costly in terms of personnel for administration, data collection, and reduction, committee preparation, annual review, HSC and OTSG coordination and manuscript preparation. The average personnel cost for these services exceeds \$500 per protocol for the WBAMC DCI. Partly due to the avalanche of regulations and increasing numbers of forms, minutes, etc., which must be maintained and distributed, the supply costs for paper, clips, staples, folders, and other strictly administrative materials have risen to an average of \$31 per protocol per year.

TDY for minimal continuing education and mission-essential training was granted. The department provided no TDY trips for any investigator to present findings at professional meetings, but funding may be available in FY82 for this purpose.

The modest increase in numbers of protocols accepted and completed, and in publications and presentations continue to attest to the value of stabilization as noted in the FY78 report. Stabilization of principal investigators continues to be a problem as witnessed partially by the number of terminated protocols and a lower completed figure than FY80. The improved funding and equipment postures were partially responsible for the largest annual increase in the number of new protocols in the history of the DCI. Several of these ongoing protocols are extremely ambitious and reflect both internal vigor and external pressures.

PROGRESS: During this fiscal year WBAMC authors had 80 articles or national/regional presentations published or accepted. This list begins on page 16. Nearly one-third of these publications and/or presentations resulted directly from protocols (C). It is important to note the DCI provided editorial and/or statistical assistance on many of the remainder. A tabulation of pertinent workload and dispositions compared to budget (not adjusted for inflation) for the past six years follows: (FY77 and 7I have been combined, but adjustment to 12 months is shown in parentheses)

	Protocols Ongoing at start FY	New Protocols Submitted During FY	Total Protocols	Protocols Completed During FY	Protocols Terminated During FY	Publications and Presentations	OMA Budget
FY76	49	32	81	12	16	48	\$20,471
FY77 & 7T	53 (42)*	25 (20)	78 (62)	18 (14)	15 (12)	24 (19)	\$56,831 (\$45,465)
FY78	45	30	75	3	9	28	\$35,923
FY79	63	43	106	9	14	46	\$34,392
FY80	83	41	124	25	25	63	\$60,134
FY81	74	59	133	16	17	80	\$86,351
FY82	100						

*Figures in parentheses represent adjustment to a base of 12 months.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 78/15 Status: Ongoing

Title:

Penicillin Alone vs Ampicillin and Gentamicin in the Treatment of Group B Streptococcal Sepsis

Start Date: 1978 Est Comp Date: Mar 1982

Principal Investigator:

Facility:

R.J. Frederick, PhD, DAC

Dept/Sec: Immunology Svc, DCI Assoc Investigators

Key Words:

Streptococci; antimicrobial agents

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost: FY81 and	Review Results
Study Objective	(Accumulative) \$0(2732)	

To determine the in vivo and in vitro killing rates of these antibiotics.

Technical Approach:

Scintillation counting will be used for in vitro studies. Serial blood cultures will be used for in vivo studies with a rabbit model.

Progress:

In vivo responses to penicillin tolerant strains of group B streptococci were monitored in the rabbit model for early-onset streptococcal sepsis. New Zealand white rabbits were injected intravenously with cell suspensions of radiolabeled, log phase bacteria with and without a three-hour exposure to penicillin. Clearance rates were monitored by measuring the disappearance of radiolabel from blood samples taken in a continuous sampling technique at ten second intervals. Clearance rates were measurably different (See Table 1) with the treated cells having nearly double the $t_{1/2}$ of untreated cells. Pre-immunization of the animals resulted in an increase in $t_{1/2}$ of untreated bacteria while that of the treated bacteria decreased.

Table 1. Clearance rates of penicillin treated and untreated group B streptococci.

GROUP B STREPTOCOCCI TYPE 1a (BAMC 11)
IN VIVO CLEARANCE RATES

CULTURE	IMMUNIZED	SLOPE	$t_{1/2}$ (Sec)
LOG PHASE	-	-0.0070	46
	+	-0.0052	64
PENICILLIN* TREATED	-	-0.00334	82
	+	-0.0077	41

*150 units/ml for three hours at 37°C

Previous work demonstrated the continued morphological integrity of the bacteria after a three hour exposure to penicillin. Although the structural integrity is maintained and only a ten percent loss of cell viability occurs, cell wall constituents are released and the average cell diameter increases approximately 20 percent.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 78/22 Status: Completed
Title:

The Efficacy of Active Immunization to Group B Streptococcal (GBS) Organisms in Preventing GBS Sepsis

Start Date: 1978 Est Comp Date:
Principal Investigator: Facility:

R. J. Frederick, PhD, DAC

Dept/Sec: Immunol Svc, DCI Assoc Investigators
Key Words:

Streptococci; Immunization

Accumulative MEDCASE Est Periodic
Cost OMA Cost: \$495(3232) Review Results
Study Objective:

To determine if active immunity will prevent acquisition of disease and/or prevent and/or blunt the clinical parameters of sepsis.

Technical Approach:

A rabbit model is being used in this study. Rabbits are immunized with GBS until they have a "+" CIE to GBS antigen. Once a "+" titer is demonstrated, the animals are injected with both live and killed organisms. CBCs, blood gases, and temperatures are followed closely. If death occurs, histological examination of tissue is being performed.

Progress:

A manuscript has been completed for publication and is awaiting internal review before submission. New Zealand white rabbits were shown to be quite susceptible to acute group B streptococcal bacteremia. A one-week immunization regimen using formalin treated type Ia or III group B streptococci produced a strong response in adult rabbits as measured by assay for anti-group B carbohydrate antibody. When type Ia GBS immunized rabbits were challenged with live cultures of the homologous type Ia strain, a reduced death rate occurred for up to four days. When type III GBS were used in the short course immunization regimen, the protection against the non-homologous type Ia strain was improved. Immunization with the type 090R strain did not protect against a type Ia GBS challenge. These results offer direct evidence against group specific protection and suggest a possible non-type specific antibody response to whole cell immunization that protects against a non-homologous type GBS bacteremia.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/01 Status: Ongoing

Title:

Role of Deoxyribonucleic Acid Attachment to Cell Membrane in the Regulation of Bacterial Growth

Start Date: 1979

Est Comp Date: Sept 1982

Principal Investigator:

Facility:

R.J. Frederick, PhD, DAC

Dept/Sec: Immunol Svc, DCI

Assoc Investigators

Key Words:

Deoxyribonucleic acid; cell membrane

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:\$825(3152)Review Results

Study Objective:

To isolate and examine specific deoxyribonucleic acid (DNA) sequences associated with bacterial cytoplasmic membranes.

Technical Approach:

Our initial experiments are designed to analyze the effect of different restriction enzymes on isolated nucleoids. These are the folded chromosome of the bacteria which can be isolated in their compact state while retaining the membrane association. The procedure can be done simply with reasonable yields under salt and pH conditions which will facilitate endonuclease treatments. Once isolated, the tritium labeled nucleoids (i.e. the entire chromosomes) will be digested with commercially available restriction endonucleases. These enzymes cleave the DNA molecules at specific nucleotide sequences resulting in specific fragments which can subsequently be separated by agarose gel electrophoresis and resolved on x-ray film by autoradiofluorography. Membrane associated fragments will be purified by fractionation using the magnesium-sarkosyl crystal separation technique. The fragments will be recovered by standard techniques and analyzed by agarose gel electrophoresis. Once the specific sequences have been resolved, we will begin to identify what regions of the chromosome are involved and under what conditions. The relationship of the attachment to bacterial growth may then be examined by varying the growth conditions of the organisms, using appropriate mutant strains and in the presence of various antibiotics.

Progress:

Much of the anticipated work on this protocol for the 1981 fiscal year was preempted to support other protocols in the department and the training of a new technician. This notwithstanding, the technique for the assessment of DNA restriction fragment size determinations has been worked out. Plans have been made to write a computer program to assist in the data reduction and analysis of results.

Various E coli mutant are now being screened for use in this protocol. Of particular interest are conditional lethal, temperature sensitive strains that are separated at the restrictive temperature. Preliminary results indicate that these strains may also be cold sensitive. Experiments are now ongoing to further demonstrate this. If our preliminary observations can be substantiated, these strains will be examined for membrane structural changes and for alterations in the association of the membrane with the bacterial chromosome.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/07 Status: Ongoing
Title:

Synthesis of Inhibitors of the Shikimate Pathway for Investigation
As Potential Antimicrobial Agents

Start Date: 1979 Est Comp Date: Sep 82
Principal Investigator: Facility:

D.O. Rauls, PhD, DAC

Dept/Sec: Chemistry Svc, DCI Assoc Investigators
Key Words:

Shikimate; Antimicrobial agents

Accumulative MEDCASE Est Periodic
Cost OMA Cost: \$590(95) Review Results

Study Objective:

The 5-alpha and 5-beta fluoro analogs of shikimic acid will be synthesized as potential irreversible inhibitors of the pathway responsible for aromatic acid synthesis in microorganisms. The compounds will then be evaluated for antibacterial activity using a standard antibacterial screen.

Technical Approach:

The desired 5-fluoro analogs of shikimic acid will be synthesized by established synthetic techniques. The antimicrobial activity will be determined using standard assays. The anticipated limiting factors appear to be related to the potential lability of the products.

Progress:

Preparation of the protected intermediate methyl 5-acetyl-3,4-isopropylidene shikimate was accomplished. However, bromination of this intermediate with n-bromosuccinimide did not proceed to the desired 5-bromopropduct. Gas chromatography-mass spectrometry indicated that an additional reaction with subsequent elimination took place giving an aromatic product. Attempts to modify the carboxyl group of shikimic acid in order to reduce steric hindrance at the 5-position have been partially successful and will be pursued further in the following year.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 8073 Status: Ongoing

Title:

Maternal Serum and Urinary Steroid Concentrations During Contraction Stress Testing

Start Date: 1 Oct 81 Est Comp Date: 1983

Principal Investigator: Facility:

L.L. Penney, COL, MC

Dept/Sec: C, Dept Clinical Invest Assoc Investigators

Key Words:

Cortiso; Estriol; Oxytocin

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost:	Review Results

Study Objective:

To determine if any changes occur in maternal serum steroid concentrations during contraction stress testing, and if so, are they of predictive value in regard to fetal outcome.

Technical Approach:

All patients admitted for contraction stress testing will be asked to participate. A two-hour urine specimen prior to beginning and another immediately from starting the oxytocin will be collected. Three to five cc of venous blood will be drawn from the arm opposite the IV infusion at 0,30,60,90 and 120 minutes of the test. The blood will be drawn in three 1 cc aliquots from the same venipuncture at five minute intervals around each drawing time and the serum combined in equal volume to compensate known variabilities in serum estriol. Specimens will be analyzed for unconjugated and total estriol and an aliquot frozen for possible analyses of cortisol, ¹⁶OH progesterone and other steroids which are being proposed as indicators of fetal well being. All specimens from positive, equivocal, or, in retrospect, false negative tests, will be analyzed following randomization assignment. Twenty negative studies will be used to compare mean urinary and serum levels at each time period from controls and study group patients. Any significant differences will be correlated in an attempt to define equivocal, false positive and false negative results.

Progress:

To date manpower constraints have prohibited institution of this protocol.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/31 Status: Ongoing
Title:

Transfer of ^{131}I from Male to Female During Sexual Intercourse

Start Date: April 1981 Est Comp Date: Sept 82
Principal Investigator: Facility:
CPT Michael L. Smith, PhD

Dept/Sec: Dept Clinical Invest Assoc Investigators
Key Words:

^{131}I ; Spermatogenesis

Accumulative MEDCASE Est Periodic
Cost OMA Cost: \$405 Review Results
Study Objective:

^{131}I is often given to patients who have had their thyroid removed because it contained a malignant tumor. The diffusion of ^{131}I to the semen of male patients and subsequent transfer to female sexual partners is not known. The purpose of this study is to determine if ^{131}I given to thyroidectomized and normal male rats is concentrated in the semen and subsequently transferred to female rats during sexual intercourse. Also the effects of the ^{131}I on spermatogenesis will be investigated.

Technical Approach:

Male rats will be divided into four groups.

Group 1: Five controls, no procedures.

Group 2: Five thyroidectomized rats, no procedures

Group 3: Five thyroidectomized rats, receive 1 mCi Na ^{131}I .

Group 4: Five nonthyroidectomized rats, " " "

Rats will be allowed to breed and both the male and their female partners will be monitored with a single channel spectrometer for radioactive uptake and decay. The male rats will be killed after one month and rete testes fluid and testicular biopsy will be examined for abnormal sperm morphology.

Progress:

Gerald Parker, DVM, perfected the thyroidectomy technique. He was transferred to Korea in June 1981. The project has been delayed until Wayne O'Brien, DVM, has an opportunity to learn the technique.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/32 Status: Ongoing

Title:

Polyamines as Chemical Markers of the Response of Patients Being Treated for Cancer

Start Date: Jan 82 Est Comp Date: Jan 84

Principal Investigator:

Facility:

CPT Michael L. Smith, PhD

Dept/Sec: Dept Clinical Invest Assoc Investigators

Key Words:

Polyamines

Accumulative MEDCASE Est Periodic

Cost

OMA Cost: \$467

Review Results

Study Objective:

Our objective is to see if serum and urinary polyamines can be used as tumor markers to follow the progress of patients being treated for cancer.

Technical Approach:

Patients with carcinoma of the colon or ovary will be used for the study. Serum and urine polyamines will be measured before, during, and after treatment. Polyamine levels and distributions will be compared to clinical signs and evaluated for clinical usefulness.

Progress:

Supplies have been received and a possible assay has been developed. No patients have been entered at present. Patients should be entered in 1982.

Detail Summary Sheet

Date: 1 Oct 82 Prot No: 81/33 Status: Ongoing
Title:

Study of the Size and Charge Heterogeneity of Prolactin in Human Seminal Plasma and Spermatozoa

Start Date: April 1981 Est Comp Date: Dec 1982
Principal Investigator: Facility:

CPT Michael L. Smith, PhD

Dept/Sec: Dept Clinical Invest Assoc Investigators
Key Words:

Prolactin; Seminal fluid; Spermatozoa

Accumulative MEDCASE Est Periodic
Cost OMA Cost: \$532 Review Results
Study Objective:

Prolactin in physiological fluids exists in several forms which differ in molecular weight or molecular charge. Our objective in this study is to identify these forms of prolactin in seminal plasma and spermatozoa and to quantitate them. Identifying and quantitating these forms of prolactin may eventually lead to an understanding of their roles in semen and fertility.

Technical Approach:

Semen samples from males undergoing fertility evaluation will be collected. Those samples with high sperm counts will be saved. Three aliquots of each sample, (1) semen, (2) seminal plasma, and (3) sperm extracts, will be fractionated by sephadex chromatography and the molecular weight distribution of prolactin will be determined by radioimmunoassay of the fractions. The charge heterogeneity will be shown by isoelectric focusing and radioimmunoassay.

Progress:

Pooled serum, semen, and seminal plasma from four patients were collected. After clinical tests were completed the remainder of the samples were subjected to G100-sephadex chromatography. The fractions were concentrated and the prolactin content determined by radioimmunoassay. Presentations and publications are presented in part below with a summary:

Presentation: Third International Congress on Human Prolactin.
Athens, Greece - 26-29 Oct 1981.

Publication: Smith ML, Lugman WA, Fariss BL: Size Heterogeneity of Immunoreactive Prolactin in Stored Semen and Seminal Plasma. Arch Andrology 7:259-262, 1981.

Summary: Freeze fracturing semen produced a molecular form of immunoreactive prolactin that was associated with sperm. The function and bioreactivity of this protein was not determined, but evidence from previous studies suggest that it has a role in capacitation.

Publication. Portions of the above study and a time study on eight separate samples collected for infertility evaluation were included in the following review paper which was requested by the editor of Arch Andrology; Smith ML and Lugman WA: Review: Prolactin in Seminal Fluid, Arch Andrology, submitted Dec 1981.

Future investigations - This protocol will be continued with a more detailed study of the size heterogeneity of sperm associated prolactin by HPLC, radioimmunoassay, and bioassay. The charge properties of sperm and seminal plasma prolactin will be studied also.

Abstract: Smith, ML, Lugman WA, Penney LL: . Prolactin in Semen and Seminal Plasma. Neuroendocrinology Ltrs 3:322, 1981.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/34 Status: Ongoing
Title:

Location of Prolactin, HCG, LH, and FSH in Human Semen: An
Immunocytochemical Study

Start Date: Dec 1981 Est Comp Date: Mar 1983
Principal Investigator: Facility:

CPT M.L. Smith, PhD

Dept/Sec: Dept Clinical Invest Assoc Investigators
Key Words:

Prolactin; Human Chorionic Gonadotropin; Luteinizing Hormone;
Follicle-stimulating hormone; Immunocytochemistry

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

The hormones prolactin, HCG, LH, and FSH have been found in semen. HCG and some prolactin is known to be associated with spermatozoa. This study proposes to determine the distribution of these hormones between oval spermatozoa, other morphological cells, and seminal plasma. This will be done by immunofluorescent techniques, light microscopy, and electronmicroscopy.

Technical Approach:

Semen will be collected from volunteers. Sperm will be separated, washed, then subjected to Sternberger's peroxidase antiperoxidase reaction. They will be observed and photographed using light microscopy. If hormone binding is observed, the sperm will also be examined by electron microscopy. Hormone distribution will be determined from electron micrographs.

Progress:

Most supplies have arrived and one subject has volunteered for the study. No results have been obtained.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/45 Status: Ongoing
Title:

Inhibition of the Uterine Vascular Effects of 1/β-Estradiol with the H2 Receptor Antagonist Cimetidine Cortisol; an Adrenergic Blocking Agent, Phentolamine; and Cycloheximide

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Dept Clinical Invest Assoc Investigators
Key Words:

1/β Estradiol; uterine blood flow; cimetidine; cortisol;
phentolamine; cycloheximide

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To quantify uterine blood flow responses two hours after a standard stimulating dose of 1/β estradiol given IV to oophorectomized rabbits pretreated with one of the specified agents.

Technical Approach:

The experimental model used in our previous work, Protocol 78/25, and in a current submission for publication, "1/β-Estradiol Stimulation of Uterine Blood Flow in Oophorectomized Rabbits with Complete Inhibition of Uterine RNA Synthesis" will be used to determine uterine blood flow with microspheres at time zero and two hours after estradiol, 10 μg/kg IV, in animals pre-treated with cimetidine 10 mg/kg; cortisol 20 mg/kg; phentolamine 10 mg/kg or cycloheximide 4 mg/kg. Twelve animals will be studied in each group and every animal will serve as its own control for comparison by paired t-test within groups.

Progress:

This newly approved protocol has not been activated.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/47 Status: Ongoing
Title:

Variability of Estradiol Induced Increases in Uterine Blood Flow as
a Function of Time Post-oophorectomy

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Dept Clinical Invest Assoc Investigators
Key Words:

1/8 estradiol; uterine blood flow

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To establish the lack of responsiveness of uterine blood flow to
estradiol stimulation in rabbits oophorectomized longer than 50 days.

Technical Approach:

We have recently completed a study of the effects of Actinomycin D
on estradiol-induced increases of uterine blood flow in
oophorectomized rabbits. During that experiment, a delay in
shipping labeled microspheres necessitated study of a small group of
control animals 50 days post-operatively as opposed to between 1-5
weeks as had been the case. At 50 days an increase in uterine blood
flow 2 hours following estradiol, 10 µg/kg, was no longer
demonstrable. Such a change with time has not previously been
reported. We wish to repeat the study with sufficient numbers of
animals to confirm or refute this observation.

Progress:

This newly approved protocol has not been activated.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/48 Status: Ongoing
Title:

Variability in Quantifiable Uterine Cytosolic and Nuclear Estrogen Receptors as a Function of Time Following Oophorectomy in Rabbits.

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Dept Clinical Invest Assoc Investigators
Key Words:

17 β estradiol; estrogen receptors

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost: \$518	Review Results
Study Objective:		

To correlate the amount of receptor present with the degree of blood flow response to 17 β estradiol.

Technical Approach:

If protocol 81/47 confirms a diminished response of uterine blood flow to 17 β estradiol, as a function of time following operation, this study will be conducted. Since a decreased response is in a sense natural inhibition a quantification for the receptors should aid in elucidating the basic mechanism. In addition to the cytosolic receptor, eosinophilic and α adrenergic receptors, as well as any others suggested by Protocol 81/45 will be examined by standard techniques detailed in the references. For each receptor 5-8 animals will be studied at 20-40 days following operation and another 5-8 at 50-80 days.

Progress:

Preliminary work on methodology has been started. Further work is pending initiation of Protocol 81/47.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/53 Status: Ongoing
Title:

Prostacyclin Synthetic Capability of Thoraco-Abdominal Aortic Dacron
Graft One Year Post-Surgery

Start Date: Est Comp Date:
Principal Investigator: Facility:

D.O. Rauls, PhD, DAC

Dept/Sec: Dept Clinical Invest Assoc Investigators
Key Words:

Prostacyclin; aortic grafts; neointima

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

The objective of this study is to determine whether or not the
neointima formed along the interior of Dacron aortic grafts develops
the capability of producing prostacyclin.

Technical Approach:

Animals with Dacron aortic grafts are available from another
protocol. The animals will be sacrificed and a portion of the graft
will be removed and incubated with ¹⁴C-arachidonate. The
prostacyclin metabolite 6-oxo-prostaglandin F_{2α} will be determined
by thin layer chromatography.

Progress:

Grafts from two animals have been studied in order to develop the
analytical procedure. Further work is needed in order to quantitate
the desired metabolite.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/09 Status: Completed
Title:

Antibiotic Prophylaxis in Intraoral Orthognathic Surgery

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ J.E. Ruggles, DC

Dept/Sec: Dept Dentistry Assoc Investigators
Key Words:

Orthognathic surgery; penicillin

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To conduct a prospective double-blind comparison of two prophylactic antibiotic regimens in patients undergoing intraoral orthognathic surgery of the maxilla and/or mandible.

Technical Approach:

Drugs to be administered in the study are Procaine Penicillin G and Aqueous Penicillin G.

a. Aqueous Penicillin G is the antibiotic agent of choice for almost all infections originating in the oral cavity, and consequently almost all infections resulting from intraoral orthognathic surgery.

b. Some controversy exists concerning what constitutes an appropriate period for prophylaxis.

(1) Peterson and Booth, in a retrospective study of patients undergoing intraoral orthognathic surgery, reported an 11.4 incidence of infection in postoperative patients who received no antibiotics.

(2) In a retrospective study by Yrastorza, the incidence of postoperative infection in patients undergoing intraoral orthognathic surgery was smaller in patients receiving no prophylactic antibiotics than for patients who received antibiotics for an average of eight days postoperatively.

(3) Zallen and Black presented what they termed current thoughts regarding the use of prophylactic antibiotics in orthognathic surgery. They recommended the use of antibiotics, but gave no recommendations concerning duration of coverage, and presented no statistical information to support their views.

(4) Burk presented guidelines for phophylactic antibiotic coverage in surgery, in which he advocated use of antibiotics only during the immediate postoperative period. However, no statistics were presented.

(5) To our knowledge, a prospective, double-blind study comparing short term and longer term prophylactic antibiotic coverage for intraoral orthognathic surgery has not been reported.

Patients eligible for inclusion in the study must be adults, eighteen years of age and older, may be of either sex, and may be civilian or military.

Patients will be excluded from the study if they give a history of allergic reaction to penicillin or other Beta Lactam antibiotic, if they have a compromised immune defense system, or if they have received antibiotic therapy within the previous fourteen days.

Total numbers of patients will be forty, divided into two groups of twenty patients.

Antibiotic Regimens:

(1) All patients will receive

- 500,000 units Procaine Penicillin G and 400,000 units Aqueous Penicillin G, I.M., one hour preoperatively.

- 2,000,000 units Aqueous Penicillin G, I.V. over 30 minutes every three hours intraoperatively.

- 2,000,000 units Aqueous Penicillin G, I.V. over 30 minutes three hours after the last intraoperative dose.

(2) Group I (20 patients) will receive

- 2,000,000 units Aqueous Penicillin G, I.V. over 30 minutes every four hours for a total of twelve doses.

(3) Group II (20 patients) will receive

- A placebo I.V. over 30 minutes, every four hours for a total of twelve doses.

Method of Followup: Followup will consist of routine postoperative care, to include observation for signs of postoperative infection. The diagnosis of postoperative infection will be made if three of the following criteria are met:

(1) Elevation of body temperature for longer than 1/2 hours postoperatively.

(2) Increased edema, induration, and erythema of wound margins and surrounding tissue.

(3) Drainage of purulent exudate from the wound.

(4) Positive serial blood cultures.

Postoperative infections, once diagnosed, will be treated with local measures and the appropriate antibiotic(s) based upon culture and sensitivity results.

All infections will be cultured utilizing both aerobic and anaerobic methods.

Progress:

This project was completed. The principal investigator is in possession of the data, but he has been reassigned and has not responded to requests from the DCI, WBAMC.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/29 Status: Completed
Title:

Serum Glucose Level in Relation to Recovery Time from General Anesthesia for Outpatient Oral Surgery Procedures.

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ D.B. Boyd, DC

Dept/Sec: Dept Dentistry Assoc Investigators
Key Words:

Glucose; general anesthesia

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To conduct a study to determine if there is a direct relationship between a patient's serum glucose level and the length of time required to sufficiently recover from a halothane general anesthetic.

Technical Approach:

An attempt to detect a relationship between serum glucose level and recovery time from patients undergoing general anesthesia will be studied. Patients eligible for inclusion in the study must be eighteen years of age or older, may be of either sex, nonpregnant, and may be dependents of military personnel or active duty military personnel. Patients must require minor oral surgery procedures which can be accomplished in forty (40) minutes or less on an outpatient basis. All patients will be NPO at least eight hours. All patients will receive general anesthesia. Blood samples for serum glucose determination will be obtained from all patients at 1-5 minute preinduction; 1-5 minutes following discontinuation of the halothane; 1-5 minutes following sufficient recovery. Intravenous fluid will be 1/2 NS via standard infusion apparatus in one half the group, and 1/2 NS/5 D in the remaining one-half. Determination of recovery time: Time shall begin upon discontinuation of the halothane; time shall run until sufficient recovery has taken place to allow release; a score of 9 or 10 on a modified post-anesthesia recovery score (PARS) as proposed by Arlow shall be sufficient recovery.

Progress:

This project was completed. The principal investigator is in possession of the data, but he has been reassigned and has not responded to requests from the DCI, WBAMC.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/25 Status: Ongoing
Title:

A Clinical Comparison of Antibiotic Steroid Preparations Used in
Post Extraction Mandibular Third Molar Sites to Reduce Associated
Post-Operative Sequellae

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC J.R. Zwolensky, DC

Dept/Sec: Dept Dentistry Assoc Investigators
Key Words:

Molar extractions; glucocorticoids; antimicrobial agents; alveolitis

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To conduct a prospective randomized, single-blind comparison of
three different antibiotic-steroid regimens used immediately
post-operatively in patients undergoing impacted third molar surgery
and their efficacy in reducing post-operative pain, trismus and
localized alveolitis.

Technical Approach:

A total of 120 patients with bilateral impacted third molars will be
divided into four groups of 40 patients each. Patients eligible for
inclusion must be adults 18 years of age or older. Males may be
military active duty or military dependent. If this study proves
significant other groups may be evaluated in the future. Patients
to be excluded from this investigation are those who give a history
of systemic disease, prior steroid therapy or are taking oral
contraceptives at time of surgery. Catellani, Harvey, Erickson and
Cherkin have shown a significant increase of incidence of localized
alveolitis (dry socket) over the general population in patients
taking contraceptives at the time of third molar surgery. Schow
reported incidence of 45 localized alveolitis in patients taking
oral contraceptives as opposed to general population.

Progress:

Patient accrual is beginning on this newly activated protocol.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/26 Status: Ongoing
Title:

Use of Op Site Transparent and Permeable Adhesive Dressing in Skin Grafting

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC D.P. Gluhm, DC

Dept/Sec: Dept Dentistry Assoc Investigators
Key Words:

Skin grafts

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

Evaluate a commercially available sterile dressing OpSite for use as a wound dressing, a barrier to infection, a vehicle for handling donor graft tissue, and its effects upon patient comfort, patient recovery time, and patient acceptance.

Technical Approach:

Patients to be included must be at least 18 years of age, military or dependents, active duty or retired, of either sex. Patients will be excluded if they give a history of previous skin graft and request a specific donor site dressing previously employed. All patients will undergo a ten minute Betadine surgical prep to the proposed graft harvest site, following standard razor prep of the area the day of surgery. All harvest sites will be defatted with acetone prior to harvest. All harvest sites will be covered with OpSite dressing prior to harvest. All split thickness and full thickness grafts will be harvested through the OpSite dressing. All residual OpSite will be removed and the area again defatted. All harvest sites will be treated with the application of a 1/100,000 epinephrine solution prior to application of OpSite dressing.

Followup will consist of routine post-op care, to include observation for signs of infection. Postoperative infection will be treated with local measures based upon culture and sensitivity. All infections will be cultured utilizing aerobic and anaerobic methods. Excess fluid accumulating beneath the OpSite dressing will be drained for C and S to prevent spontaneous leaking or rupture, following 10 minute Betadine prep. Dressing will be removed by the patients themselves while bathing on the 10th postoperative day.

Patients may shower at will following surgery, but will be instructed not to scrub the dressing. Patients will be allowed and encouraged to ambulate at will following surgery. Patients will be requested to complete a questionnaire at one week and one month following surgery.

Progress: Patient accrual is beginning on this newly activated protocol.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 75/23 Status: Terminated
Title:

Effect of a Broad Spectrum Antibiotic on the Course of Viral URI

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL R.E. Morrison, MC

Dept/Sec: Dept of Medicine Assoc Investigators
Key Words:

Upper respiratory infection; Tetracycline

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To determine in a controlled double-blind study the effect of an antibiotic on the clinical course of acute viral upper respiratory tract infections with particular attention to any beneficial or deleterious effects of the treatment with respect to secondary bacterial complications.

Technical Approach:

Patients admitted to the Acute Respiratory Distress (ARD) ward without obvious bacterial infections will be divided into two random groups. One group will receive tetracycline HCL, the other a placebo. The physician taking care of the patients, and the patients themselves, would not know whether they were receiving drug or placebo. The code would be held by the Pharmacy Service. The incidence of complications, in particular, secondary bacterial infections; the total length of fever; the general well-being; length of hospital stay; incidence of adverse drug reaction; and the total cost of treatment would be compared between the two groups.

PROGRESS: None

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 75/33 Status: Ongoing
Title:

Diagnostic Adrenal Scanning with ¹³¹I (NP59)

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC T. Brown, MC

Dept/Sec: Nuclear Medicine Svc Assoc Investigators
Key Words:

Adrenal scanning

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost:	Review Results

Study Objective:

The purpose of this study is to determine the usefulness of ¹³¹I NP59 in scanning of the adrenal glands. It will be employed for the following purposes: (a) as a screening test for detection of primary aldosterone tumor, Cushing's disease, adrenal cortical adenoma, or pheochromocytoma, (b) imaging of adrenals in patients who require adrenal venography and are allergic to contrast media, (c) detection of unilateral adrenocortical hypofunction: calcification, metastatic carcinoma, post-venography infarction, etc., (d) detection of functioning adrenal remnant after adrenalectomy for Cushing's syndrome, (e) aid in assessment of adrenocortical steroid therapy.

Technical Approach:

Patients with clinical evidence of adrenal disease will be studied upon referral from the Endocrine Service. Adrenal imaging will be performed after injection of the material to assess the presence or absence of visualization of the adrenal glands, their size and response to suppression therapy.

Progress: No patients were entered in FY81. This study is kept open to ensure the institution has an adrenal scanning agent for the unusual cases which require such a diagnostic technique.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 78/03 Status: Terminated
 Title:

Comparison of Cellular Metabolic Indices with Thyroid Dysfunction and Therapy

Start Date: Est Comp Date:
 Principal Investigator: Facility:

LTC M.E. Sellers, PhD

Dept/Sec: Dept Clinical Invest Assoc Investigators
 Key Words:

2,3-diphosphoglycerate; thyroid function tests

Accumulative MEDCASE Est Periodic
 Cost OMA Cost: \$0(200) Review Results
 Study Objective:

To clarify the relationship and clinical usefulness of systolic time intervals as an index of cardiac output and myocardial contractility, O₂ consumption at rest and at steady state exercise, 2,3-diphosphoglycerate (2,3-DPG), measurements in hyperthyroid, euthyroid and hypothyroid patients and to evaluate the possible use of these parameters in monitoring therapeutic interventions.

Technical Approach:

Prior to initiation of therapy, hypothyroid and hyperthyroid patients will be screened for factors influencing 2,3-DPG levels. The patients will then undergo testing of hematocrit, hemoglobin, 2,3-DPG, pO₂, pCO₂, pH, bicarbonate, serum CO₂, O₂ consumption at rest and exercise steady state, and systolic time intervals at rest. Hyperthyroid patients will be tested prior to therapy, after one week of propranolol therapy and at time of achieving a clinical and thyroid function euthyroid state by means of ¹³¹I therapy and/or prophythiouracil or methamazole. Hypothyroid patients will be tested prior to therapy and at time of achieving a clinical and thyroid function euthyroid state by means of levothyroxine therapy. Euthyroid goiter/nodule patients will be tested prior to therapy and at a therapeutic steady state approximately two months after initiation of suppression therapy with levothyroxine. Factor analysis will be applied to clinical indices, thyroid function tests, 2,3-DPG, systolic time intervals and resting and exercise steady state O₂ consumption with correlations being made to thyroid dysfunction state and therapeutic measures utilized.

Progress: None

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/05 Status: Completed

Title:

Technetium-99m-pyridoxylidoneglutamate (Tc-99m-PG) for Diagnosis of Hepatobiliary Disease

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC H.W. Henry, MC

Dept/Sec: Nuclear Medicine Svc Assoc Investigators

Key Words:

Hepatobiliary scanning

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost:	Review Results

Study Objective:

To evaluate the clinical efficacy of Tc-99m-PG as a diagnostic hepatobiliary and gallbladder agent. Tc-99m-PG is presently being evaluated for its ability to provide clinically useful information regarding biliary tract and gallbladder disease processes. This radionuclide has already been shown to be valuable in the assessment of hepatobiliary function, diagnosis of acute cholecystitis, evaluation of gallbladder dysfunction, and in differentiation of hepatocellular disease from extrahepatic obstructive jaundice.

This additional diagnostic agent could provide more rapid diagnoses in diseases of the biliary tract and gallbladder than with the standard methods presently available. Earlier diagnoses of abnormalities could decrease patient suffering overall and particularly in the acutely ill.

Tc-99m-PG has been demonstrated to have a wide margin of safety, thereby avoiding the risk of reactions. A high incidence of reactions, including fatal reactions, is known to occur with intravenous cholangiographic contrast materials utilized in conventional radiography. The actual incidence of reactions to intravenously administered cholangiographic contrast media overall is not accurately established since no consistent efforts have been made to report nonfatal reactions. The incidence of fatal reaction following intravenous cholangiography is approximately 0.0025 or 1:40,000. Because of the rapid blood clearance of Tc-99m more rapid diagnoses may be made in acute cholecystitis (i.e., within one hour), whereas, conventional radiographic methods may require several hours. Quantitative assessment of hepatobiliary function is possible with Tc-99m-PG. Tc-99m-PG may allow improvised visualization of the biliary system, even when the serum bilirubin level is mildly elevated. Lack of β - radiation allows the use of doses up to 15 mCi giving statistically more valuable information about biliary function than with I-131-rose bengal.

Technical Approach:

The patient population for the study will consist of active duty, retired, and appropriate dependent personnel who have suspected acute or chronic hepatobiliary disease processes.

Patients who are pregnant, lactating, or who are under the age of 18 years will not be studied unless the indications for the study and the benefit to be gained outweigh the potential risk to the patient. Female patients of childbearing age will be studied within approximately 10 days following the onset of menses. Patients after 10 days menses will be evaluated for benefit versus risk. A series of patients who fulfill the above criteria will be injected intravenously with Tc-99m-PG. The adult dose will consist of approximately 15 mCi. For patients under 18 years of age that dose will be calculated according to the weight or approximate body surface area of the patient. Each patient study will be carried out under the supervision of a physician. The instruments used for detection will be the gamma scintillation cameras located at the William Beaumont Army Medical Center, Nuclear Medicine Service.

Each patient will be studied following a 4-5 hour period of fasting when possible. Following intravenous administration of the Tc-99m-PG sequential scintiphotos will be obtained at 5 minute intervals for up to one hour following injection. Simultaneous computer acquisition of the data will be obtained for further analysis. Nuclear images will be made and stored on film and/or on magnetic tape or data storage disks. Curve plot data can be subsequently derived from this information when appropriate.

In selected patients who have suspected chronic gallbladder disease, delayed images may be obtained at 2-4 hours post-injection when deemed necessary. If gallbladder dysfunction is suspected in patients who have chronic symptoms but who have been shown not to have calculi by routine oral cholecystography, evaluation of gallbladder emptying may be obtained by intravenous injection of Kinevac (Sinacalide for injection - manufactured by E.R. Squibb and Son, Inc. and currently used in routine oral cholecystography). The dose recommended by the manufacturer is 0.02 mcg. per kg. This methodology offers the advantage of a standardized, precise and reproducible quantitative assessment of gallbladder contractility (better than oral fatty meals etc., used in conventional radiographic techniques in the past). This will allow computer analysis and printout of data for determination of a washout curve as gallbladder emptying occurs. Prescription forms, patient charts, and consultation forms will be used to record pertinent data.

Progress: Twenty-three patients were entered. No untoward or adverse effects occurred. Superior hepatobiliary scanning agents are available (see Protocol 81/11) and no more patients will be studied on this protocol.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/13 Status: Terminated
Title:

Incidence of HL-A B2/ Positivity in "Idiopathic" Aortic Insufficiency

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Svc Assoc Investigators
Key Words:

Aortic Insufficiency

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine if "idiopathic" aortic insufficiency can be an isolated manifestation of the spectrum of HL-A B2/ associated syndromes.

Technical Approach:

Aortic insufficiency has been associated with ankylosing spondylitis, psoriatic arthritis, ulcerative colitis, Reiter's syndrome and incomplete Reiter's syndrome. It occurs in 1-4 of patients with ankylosing spondylitis. The various manifestations of these syndromes present asynchronously, some occurring years before the complete syndrome and others years later. With incomplete Reiter's Syndrome arthritis is the major manifestation to occur. There is a high association between HLA B2/ tissue type and ankylosing spondylitis, psoriatic arthritis, ulcerative colitis, Reiter's Syndrome, and post-dysenteric arthritis. With the known variation in presentation of the different aspects of the disease, it is possible that isolated events occur without development of any other manifestation. It has been shown that anterior uveitis, which is frequently associated with these diseases, can present without arthritic pathology. There is an increased HLA B2/ antigen associated.

The purpose of this study is to try to identify a genetic subgroup among people with isolated aortic insufficiency who represent a single manifestation of the HL-A B2/ positive spectrum of disease. Charts of patients with AI from the Cardiology and Internal Medicine Clinics of this hospital will be reviewed to rule out a history of rheumatic fever, syphilitic aortitis, SBE, and for presence of an arthritis history. Physical examination will be used to confirm univalvular disease and absence of Marfan's syndrome. Those

patients that fit the criteria will have HL-A tissue typing performed which requires one vial of blood. Appropriate x-rays will be taken when history and physical examination indicate. At least 30 to 50 patients will be needed in the study to have meaningful results. It should take from nine months to one year to accumulate the patients and laboratory data. Controls will consist of people with acute insufficiency with definite etiology.

Progress: None

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/14 Status: Terminated
Title:

Clearing of Bacteria from Sputum of Patients with Chronic Bronchitis
or Pneumonia Following Antibiotic Therapy

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT H.M. Richey, MC

Dept/Sec: Dept Medicine Assoc Investigators
Key Words:

Pneumonia; Bronchitis; Sputum

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

The objective of this study is to determine the amount of time required for sputum from patients with chronic bronchitis and or pneumonia to become clear after antibiotic therapy is initiated.

Technical Approach: The rate of clearing of bacteria from urine and blood following antibiotic therapy has been described. In respiratory disease the rate of clearing of clinical symptoms and radiographic abnormalities is known. However, the rate of clearing of bacteria from sputum in patients with infected airways or pneumonia is not known. The purpose of this study is to determine that rate of clearing. Correlation with clinical status and response to therapy will be analyzed.

Patients admitted to the medical services of William Beaumont Army Medical Center with chronic bronchitis or pneumonia will have a sputum collected for gram stain and culture on admission. After appropriate antibiotics have been begun, subsequent sputum samples will be collected for gram stain at 5, 12, 24 and 48 hours after admission and the presence or absence and type of bacteria present will be noted.

Patients admitted with the above diagnoses will be used regardless of age and sex. Thirty to fifty patients will be used. No controls will be included. The approximate time to completion will be about six months.

Progress: None

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/15 Status: Terminated

Title:

SWOG /433: Stage I and II Non-Hodgkins Lymphoma

Start Date: Est Comp Date:

Principal Investigator: Facility:

MAJ P.C. Farley, MC

Dept/Sec: Oncology Svc Assoc Investigators

Key Words:

Lymphoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To compare the remission rate, remission duration and survival in patients with non-Hodgkin's lymphoma, pathologic stages I, IE, IIE treated with extended field radiotherapy (supradiaphragmatic mantle or abdominal field) alone, with extended field radiotherapy plus combination chemotherapy.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress:

No patients were entered. This protocol has been closed by SWOG.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/21 Status: Terminated
Title:

SWOG 7521: Adjuvant Melanoma

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Oncology Svc Assoc Investigators
Key Words:

Melanoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine the efficacy of BCNU, hydroxyurea, and imidazol carboxamide (BHD) in preventing the recurrence of disease and prolonging the survival of patients with primary malignant melanoma who have received definitive surgical treatment for their primary lesions, have no evidence of residual disease but in whom by the clinical and pathological characteristics of the primary lesion can be predicted to have a high incidence of recurrence.

To determine the efficacy of combination chemotherapy (BHD) with and without BCG in preventing the development of metastases and prolonging the disease-free interval and survival of patients with recurrent malignant melanoma which has been surgically excised (minimal residual disease). To determine the immunocompetence of patients with malignant melanoma and any correlation with prognosis.

To determine the influence of chemotherapy and chemoimmunotherapy upon the immunocompetence of these patients with malignant melanoma.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress: No patients were entered. This study has been closed by SWOG.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/24 Status: Terminated
Title:

SWOG 7532: Combined Modality for Recurrent Breast Cancer

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Oncology Svc Assoc Investigators
Key Words:

Carcinoma, breast

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

Establish the survival of breast cancer patients when treating the first recurrence with a coordinated hormonal chemotherapeutic approach. Determine the efficacy of a response to the antiestrogen Tamoxifen in predicting response to ablative surgery. Correlate hormonal manipulations with estrogen and progesterone receptors where possible.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress:

No patients were entered. This study has been closed by SWOG.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/25 Status: Terminated
Title:

SWOG 7703: Treatment in Combination with BCNU, DTIC, or
Procarbazine in Patients with Malignant Gliomas of the Brain

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Oncology Svc Assoc Investigators

Key Words:

Glioma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

The purpose of this study is to compare the effectiveness of
radiation therapy plus BCNU, radiation therapy plus DTIC, and
radiation therapy plus Procarbazine for remission induction,
duration of remission, and survival in patients with malignant
gliomas of the brain.

Technical Approach:

The details are lengthy and specified in the original SWOG
protocol. Duplicates are kept on file in the Clinical Investigation
Department, WBAMC, and are available upon request.

Progress:

No patients were entered. This protocol has been closed by SWOG.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/28 Status: Ongoing
Title:

SWOG 7713: Chemotherapy in Non-Hodgkins Lymphoma CHOP vs CHOP + Levamisole vs CHOP + Levamisole + BCG for Remission Induction Therapy

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Oncology Svc Assoc Investigators
Key Words:

Lymphoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To compare the effectiveness, in terms of rate of response two chemo-immunotherapy regimens (CHOP + Levamisole vs CHOP Levamisole BCG) against CHOP for remission induction in previous untreated patients with non-Hodgkin's lymphoma.

For patients proven to be in complete remission after induction, to compare the duration of documented complete response obtained by continued maintenance immunotherapy with Levamisole vs no maintenance therapy.

For patients with impaired cardiac function (not eligible for treatment with Adriamycin), with mycosis fungoides, or with only a partial response to 11 courses of treatment with CHOP-Levamisole-BCG, to estimate the complete response obtained by continued chemoimmunotherapy with CHOP - Levamisole.

To estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used.

To continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hematopathology review of diagnostic material from all cases.

To establish baseline and serial data on immunologic statute in both chemoimmunotherapy groups.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress:

— One patient has been entered and is currently in remission.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/34 Status: Ongoing
Title:

SWOG 7804: Adjuvant Chemotherapy with 5-FU, Adriamycin and
Metomycin C (FAM) vs Surgery Alone for Patients with Locally
Advanced Gastric Adenocarcinoma Phase III

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Oncology Svc Assoc Investigators
Key Words:

Carcinoma, gastric

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine the efficacy of adjuvant chemotherapy with
5-Fluorouracil, Adriamycin and Mitomycin-C (FAM) on the disease-free
interval and survival of patients with TNM stage-groups IB, IC, II
and III gastric adenocarcinoma compared to potentially curative
surgery alone.

Technical Approach:

The details are lengthy and specified in the original SWOG
protocol. Duplicates are kept on file in the Clinical Investigation
Department, WBAMC, and are available upon request.

Progress:

No patients were entered in FY81.

Detail Summary Sheet

Date: 1 Oct 81	Prot No: 79/35	Status: Ongoing
Title: SWOG 7811: Brain Metastases Phase III		
Start Date:	Est Comp Date:	
Principal Investigator:	Facility:	
LTC P.C. Farley, MC		
Dept/Sec: Dept Medicine, Oncology	Assoc Investigators	
Key Words:		

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost:	Review Results
Study Objective:		

To determine the effectiveness of combined radiation therapy and metronidazole (Flagyl) in the treatment of patients with brain metastases from primary malignancies outside the central nervous system, compared with radiation therapy alone, as determined by objective response (brain and/or CAT scan) and/or increase in functional neurologic level and duration of response.

To determine the toxicity of multiple dose administration of metronidazole and radiation therapy.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress:

No patients were entered in FY81.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/35 Status: Ongoing

Title:

SWOG 7823/24/25/26: ROAP-ADOAP in Acute Leukemia, Phase III

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Leukemia

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To compare the efficacy of the 4-drug combination chemotherapy regimen, ROAP (Rubidazone, vincristine, arabinosyl cytosine, and prednisone) to ADOAP (the same combination using Adriamycin in place of Rubidazone) in adult acute leukemia, as determined by remission rate, remission duration and survival.

To determine the comparative toxicity of these regimens.

To determine whether late intensification therapy at 9 months after complete remission will improve long term, disease-free survival.

To determine whether immunotherapy using levamisole for 5 months after 12 months of complete remission on chemotherapy improves disease-free survival.

To determine reproducibility of the FAB/histologic classification and correlation to response to therapy in 200 consecutive cases of acute leukemia.

To study the effects of intensive supportive care in the management of acute leukemia.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress:

Two more patients were entered in FY81. Three remain in evaluation and one has expired.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/1 Status: Complete

Title:

A Comparison of Development of Sensitivity to Penicillin in Normal and Atopic Individuals

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy Assoc Investigators

Key Words:

Atopy; Penicillin

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
---------------------------	---------------	-------------------------

Study Objective:

To determine if people with allergic disease manufacture more IgE antibody after receiving penicillin. It would be hoped to evaluate this in the relation to normal individuals.

Technical Approach:

Patients receiving penicillin for therapeutic reasons were tested before and after administration of oral penicillin.

Progress:

The data was forwarded to the collaborating institution, FAMC, for analysis and manuscript preparation.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/8 Status: Ongoing

Title:

Evaluation of Thyroid Hormones in Alcoholic Hepatitis

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ M. Anees, MC

Dept/Sec: Dept of Medicine

Assoc Investigators

Key Words:

Thyroid hormones; alcoholism; hepatitis

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

The objective of this study is to delineate the physiology of thyroid hormone under the stress of alcoholic hepatitis. The intent is to determine if a defect in thyroid hormone metabolism exists and if so determine if the defect is a lack of deiodination of thyroxine (T4) or as a reversal of iodination.

Technical Approach:

Twenty patients classified as acute alcoholic liver hepatitis will be entered into the study. Blood (10 ml) will be drawn on the day of admission for T4, T3, and rT3 studies. These studies will be repeated two more times at weekly intervals during the course of the hospital stay. Control studies will be performed on routine thyroid function study patients considered to be normal. Statistical comparison of normal versus test patient thyroid studies will be made and evaluated.

Progress:

Patient entry is nearly complete. Data analysis is expected in FY82.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/10 Status: Ongoing

Title:

The Hematologic & Metabolic Status of Sickie Cell Trait Individuals Following Vigorous Exercise

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Sickle Cell Trait

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

The degree of sickling, hemolysis, pH change, myolysis, and hematuria will be assessed in sickle cell trait individuals as compared to normal controls while undergoing vigorous exercise.

Technical Approach:

Approximately 50-70 heterozygous sickle hemoglobin patients and a like number of controls will be observed. The appropriate blood and urine studies will be performed on these individuals at their place of training while engaged in the physical activity. Individuals may be asked to participate more than once in the study if they demonstrate any departures from normal. The phases of investigation will be (a) screen incoming black recruit population for sickle cell trait and other heterozygous sickle cell states. (b) On volunteer controls and subject individuals obtain baseline CBC, serum chemistry, hemoglobin electrophoresis and urinalysis during in-processing. (c) Identify subgroups of study subjects according to the level of hemoglobin S and degree of hyposthenuria; load of physical conditioning and body habitus. (d) Contrast the subgroups of study participants with each other and with a control group while they undergo the PT test of their training program with the following parameters: Changes in CBC, electrolytes, muscle enzymes, serum free hemoglobin, and percent of sickling of red blood cells, urinary sediment content and assay of urine myoglobin and hemoglobin (e) Records to be kept - consent form of participants. Routine WBAMC data flow sheets will be used to record results. (f) During inprocessing of recruits we hope to ask their cooperation in joining the study and will present them with a consent form describing the

need to obtain blood and urine samples. Individuals who are asked to participate on more than one training occasion will be required to sign a consent for each occasion. (g) All of the above is to be coordinated with the training command.

Progress:

This protocol is being revised and may be resubmitted as a more comprehensive study. No patients were entered in FY81.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/11 Status: Ongoing

Title:

Prospective Study of Mannitol in the Prevention of Radiographic Contrast Induced Acute Renal Failure

Start Date: Est Comp Date:

Principal Investigator: Facility:

MAJ M. Siedlecki, MC

Dept/Sec: Dept Medicine, Renal Clinic Assoc Investigators

Key Words:

Mannitol; Radiographic contrast; Acute renal failure

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
---------------------------	---------------	-------------------------

Study Objective:

The objective of this study is to perform a prospective, randomized and double-blind study of the possible protective effects of mannitol in preventing acute renal failure induced by radio contrast media.

Technical Approach:

Approximately 20 subjects in each of two groups for each procedural category will be studied. The first procedure will be intravenous pyleography, but such procedures as coronary angiography abdominal and cranial angiography may also be studied. Patients will be ages 18 and above, active duty, dependents, and retired. The patients will be randomized blindly and either receive 500 cc of dextrose, 5 percent water or 500 cc of dextrose, five percent water plus five percent mannitol within one hour of the radiographic procedure. Additional volume supplementation will be at the discretion of the attending physician. The amount and type of contrast material used, and the type of procedure, as well as additional data, will be recorded.

Progress:

The WBAMC Human Use Committee has extended approval of this protocol to continue patient entry beyond the 20 originally proposed. Observations from this study have been published and presented (See FY80 and FY81 Table of Publications and Presentations). A new principal investigator has assumed this protocol.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/15 Status: Ongoing

Title:

An Investigation into the Effects of Cromolyn Sodium on Nonspecific Bronchial Hyperactivity

Start Date: Est Comp Date: Mar 1982

Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Se+: Dept Medicine, Allergy Clinic Assoc Investigators

Key Words:

Cromolyn; Bronchial hyperactivity

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
---------------------------	---------------	-------------------------

Study Objective:

To evaluate whether cromolyn sodium administration will cause a decrease in non-specific airway hyper-reactivity. To determine if this diminution will be associated with a favorable clinical response.

Technical Approach:

Asthmatic patients will use cromolyn by inhalation in a double-blind cross-over trial. Bronchial hyper-reactivity will be monitored by monthly histamine challenges. Twenty nonpregnant adult asthmatic patients not requiring corticosteroid therapy will be selected. They will be advised of the purpose of the study and how it will be carried out. Any subject with a history suggesting a risk of renal or hepatic dysfunction will be excluded. This study will begin in October and end in March, at which time the code will be broken. If the results suggest significant benefit for cromolyn patients, the active therapy will be offered to all patients and the study continued for six more months.

Progress:

Patient entry for this protocol is nearly complete. Data analysis should be accomplished in FY82.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/18 Status: Ongoing

Title:

Clinical Evaluation of Renal Cortical Imaging Utilizing ^{99m}Tc -Kidney Scintigraph

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC T.J. Brown, MC

Dept/Sec: Dept Medicine, Nuclear Med Svc Assoc Investigators

Key Words:

Renal Scanning

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine the usefulness of ^{99m}Tc -Kidney Scintigraph in studying renal blood flow and renal anatomy. Intended for use in high resolution and/or tomographic imaging for evaluation of anatomic detail. Especially important for space occupying lesions and renal trauma.

Technical Approach:

A series of adult patients who require renal radionuclide studies for diagnostic purposes will be studied in detail and compared with our standard renal agents. The imaging protocol is as follows:

1. Rapid images of the kidneys will be obtained with an Anger Scintillation Camera during the first 30 seconds following injection of ^{99m}Tc -DMSA. These views will be used to evaluate the agent as a vascular flow agent.

2. Initially static images will then be obtained over the kidneys for the next 15 to 30 minutes to qualitatively evaluate early renal uptake of radionuclide and to determine its usefulness as a fast renal imaging agent.

3. Initially sequential static images will also be obtained at varying time intervals to evaluate the optimal imaging time for this agent.

4. After the results of the above steps are evaluated in the first 20 patients, a modified imaging protocol will be developed for the remainder of the study based upon the usefulness of the early static images and optimal imaging time.

5. For individual patients, the standard posterior views will be supplemented by oblique, lateral, anterior and pinhole views as required.

The patients to be studied under this protocol will meet the following criteria: (1) Nonpregnant and over the age of 18, unless special indications for study exist. (2) All will have either known or suspected alteration of renal function or anatomic morphology, i.e., no subject without manifest or suspected disease will be studied

Progress:

Patient accrual has been extremely slow (one to date).

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/19 Status: Ongoing

Title:

WRAMC /915 Prevention of Gonadal Damage in Women Treated with Combination Chemotherapy or Radiotherapy Below the Diaphragm for Hodgkins or nonHodgkins Lymphoma

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Lymphoma; Ova; Gonad

Accumulative MEDCASE
Cost

Est
OMA Cost: \$152(152)

Periodic
Review Results

Study Objective:

To protect the ova and follicular cells from ionizing radiation or chemotherapeutic damage and death by putting these cells at rest during active therapy.

Technical Approach:

The details are lengthy and specified in the original WRAMC protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/20 Status: Ongoing
Title:
SWOG 7827: Combined Modality Therapy for Breast Carcinoma, Phase III

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology Assoc Investigators
Key Words:

Carcinoma, breast

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
---------------------------	---------------	-------------------------

Study Objective:

1. To compare the disease-free interval and recurrence rates in estrogen receptor positive (ER+) premenopausal patients with Stage II disease, using combination chemotherapy alone versus combination chemotherapy and oophorectomy.
2. To compare the disease-free interval and recurrence rates in estrogen receptor positive postmenopausal patients with Stage II disease, using combination chemotherapy plus tamoxifen versus tamoxifen alone versus combination chemotherapy alone.
3. To compare the disease-free interval and recurrence rates in all estrogen receptor negative (ER-) patients with Stage II disease using one versus two years of combination chemotherapy.
4. To compare the effect of these various adjunctive therapy programs upon the survival patterns of such patients.
5. To correlate the ER status with disease-free interval and survival.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress:

No additional patients were entered in FY81. The four patients entered in FY80 continue in remission.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/21 Status: Ongoing

Title:

SWOG 792/128: Chemotherapy for Multiple Myeloma Phase III

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Multiple myeloma

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

1. To compare the effectiveness of four different drug combinations for remission induction in previously untreated patients with multiple myeloma. Results will also be compared with those from similar therapies in recently completed Southwest Oncology Group Studies.

2. For patients with a 1/5 percent tumor reduction; to evaluate the role of 12 months of chemotherapy maintenance with VCP or VCP plus levamisole, when compared with previous experiences.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress:

Two patients have been entered. One has expired and the other is in remission.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/22 Status: Ongoing

Title:

SWOG 7924: Multimodal Therapy for Limited Small Cell Carcinomas of the Lung

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Carcinoma, lung

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

1. To determine the efficacy of sequentially alternating, mutually noncross-resistant, multidrug regimens in remission induction and intensification therapy in patients with limited small cell lung carcinoma.

2. To determine the value of chest-radiotherapy added to intensive systemic chemotherapy in reducing chest recurrences, and in improvement of survival.

3. To determine the relative efficacy and toxicity of low-dose, extensive chest radiation when used in close chronologic sequence with systemic multiagent chemotherapeutic regimens.

4. To determine whether radiotherapy ports should be set according to tumor size prior to or after induction chemotherapy.

5. To determine the value of combined systemic chemotherapy and radiotherapy in the control of bulky chest disease.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/23 Status: Ongoing

Title:

An Evaluation of Three Rapid Nonradioisotopic Methods for the Immune Complexes in Human Disease

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy Clinic Assoc Investigators

Key Words:

Enzyme linked immunoassay; Nephelometry; Latex agglutination inhibition; Radioimmunoassay

Accumulative MEDCASE
Cost

Est
OMA Cost:\$314(314)

Periodic
Review Results

Study Objective:

To evaluate three different methods to detect immune complexes in human disease. It is hoped to find the one or two most useful methods through clinical research and in patient surveillance.

Technical Approach:

Three methods will be used to measure immune complexes: laser nephelometer, an enzyme linked assay, and latex agglutination inhibition. These will be compared to C₁Q radioimmunoassay in their ability to detect preformed human immune complexes.

Progress:

Progress has been made in the refinement of the enzyme linked assay. The study awaits a source of purified C₁Q protein.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/24 Status: Ongoing

Title:

The Development of an Enzyme Linked Assay to Measure Human Allergen Specific Antibodies of the Immunoglobulins G and M Class

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Clinic

Assoc Investigators

Key Words:

Immunoglobulins; Enzyme linked immunoassay

Accumulative MEDCASE

Est

Periodic

Cost \$4,300

OMA Cost: \$4522(4522)

Review Results

Study Objective:

To modify the enzyme linked immunoassay developed to measure allergen specific IgE antibodies to the measurement of allergen specific IgG and IgE antibodies.

Technical Approach:

Allergen will be chemically bound to polyethylene tubes or plastic microtiter plates. Highly specific rabbit antisera to IgG and IgM will have either alkaline phosphatase or galactosidase enzyme attached to it. The plates or tubes will be layered over with human allergic sera obtained at various times during allergen immunotherapy.

They will be washed and then relayered with "labeled" anti IgG or IgM. After incubation the plates or tubes will be washed. A solution containing the proper substrates for the enzyme will be added to the plates. The enzyme driven reaction will cause a colorimetric change in the solution. The results will be read visually and in a spectrophotometer. The results will be compared to the radioimmunoprecipitation method which will be performed in the usual fashion. The human sera used has been previously obtained and evaluated by the radioimmunoprecipitation at Fitzsimons Army Medical Center.

Progress:

The techniques for this study have been developed. Specimens pre- and post-allergen therapy are being collected.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/25 Status: Ongoing

Title:

Assessment of Hematologic and Neurologic Abnormalities in the Young Alcoholic Patient

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Alcoholism

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$/88(188)

Review Results

Study Objective:

To determine if hematologic abnormalities exist in the young alcoholic population in the absence of liver disease or severe nutritional deficiency. To determine the degree of intellectual impairment and presence of peripheral neuropathies especially in the young alcoholic patient.

Technical Approach:

All patients admitted for alcohol detoxification or alcoholic liver disease will be considered study subjects. No invasive procedures as bone marrow biopsy or liver biopsy will be proposed as part of this study. However, if the patient's physician obtains such a biopsy, we will use the data. CBC, SMA 12, serum folate and blood smear will be obtained routinely. Patients who are anemic will have a red cell folate and serum Fe and IBC also collected, and other studies as indicated to evaluate the anemia. In addition to the above routine evaluation, the patients will be asked to consent to the following: (1) Liver sonogram study, (2) Clinical examination by neurologist, (3) Cranial C.T. Scan (when machine is available at WBAMC), (4) WAIS Test (Weckslar Adult Intelligence Scale). Most patients consent to enter the Day Care Treatment Center for two weeks after admission for detoxification. Ideally this will be the period of time when studies are obtained.

Progress:

Patient entry has been completed. Data is being analyzed and prepared for presentation, and a manuscript is in preparation.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/28 Status: Ongoing

Title:

The Use of a New Multitest Applicator in the Evaluation of the Clinical Efficacy of Allergen Immunotherapy

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dep./Sec: Dept Medicine, Allergy Clinic Assoc Investigators

Key Words:

Immunotherapy

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
---------------------------	---------------	-------------------------

Study Objective:

To assess the value of using a new device called the multitest in the use of serial skin tests to monitor the efficacy of allergen immunotherapy.

Technical Approach:

Thirty adult patients who are to begin immunotherapy will be entered into the study. The nature and the purpose of the study will be explained to them.

Each patient will have an immunotherapy set prepared for them. This will be that which is clinically indicated for them. On the day when they begin their immunotherapy program, they will have a specimen of blood drawn. They will be tested by the prick-puncture and by the multitest device to the following: 10 serial dilutions 1:200 to 1:200,000 for their treatment mixture; dilutions of 1:100 to 1:100,000 of either ragweed or Russian thistle allergen (depending upon the patient's sensitivity). The multitest device will be placed so that the top part of the device touches an imaginary line drawn through the points of the scapula. A template will be used to assure a constant location for the titrated puncture test. For uniformity prick-puncture test will be done on the right side of the back two inches from the spine. The serum obtained prior to immunotherapy and at maintenance will be evaluated for the presence of IgE, IgG, and IgM specific antibody to ragweed and/or Russian thistle allergen.

Progress: This protocol has been delayed pending assignment of a resident physician as an associate investigator.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/31 Status: Ongoing

Title:

Direct and Indirect Radionuclide Cystography in the Detection of Vesicoureteral Reflux

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC T.J. Brown, MC

Dept/Sec: Dept Medicine, Nuclear Med Svc Assoc Investigators

Key Words:

Cystography; Vesicoureteral reflux

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

1. To detect and quantify vesicoureteral reflux.
2. To provide early detection of any deterioration in renal function.

Technical Approach:

Patients with known vesicoureteral reflux will be studied by computerized radionuclide renal imaging and direct radionuclide cystography. The radioactive pharmaceutical used will be ^{99m}Tc-DTPA. These studies will be performed on the child's regularly scheduled followup visit to the Urology Clinic, in lieu of further radiographic examinations. A flow sheet will be completed on each child that is studied and copies retained by the Nuclear Medicine and Urology Service.

Progress:

Nine patients have been entered. The data is being prepared for presentation at the Kimbrough Urological Seminars.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/32 Status: Ongoing

Title:

A Randomized Trial of Chemotherapy and Radiation Versus Radiation Alone in the Treatment of Advanced Non-small Cell Lung Cancer

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology C1

Assoc Investigators

Key Words:

Carcinoma, lung

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine the efficacy of combination chemotherapy with 5Fu, Vincristine and Mitomycin as measured by response rate and survival benefit in patients with advanced non-small cell lung cancer.

Technical Approach:

The details are lengthy and specified in the original protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress:

Fifteen patients have been entered. One has been a long-term survivor.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/33 Status: Ongoing
Title:
The Effect of Beta 2-Adrenergic Agents on Immunoglobulins

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy Clinic Assoc Investigators
Key Words:

Beta II agonists; Immunoglobulins

Accumulative MEDCASE Est Periodic
Cost OMA Cost: \$284/ (284/) Review Results

Study Objective:

To establish in an animal model if the effects of beta-2-adrenergic agents on immunoglobulin levels are due to defects of synthesis or increased catabolism.

Technical Approach:

Laboratory white rats will be used for this experiment. They will be grouped in units of ten animals according to the following plan.

- a. Control groups, no medication
- b. Terbutaline 125 mcg/kg twice daily for 4 weeks
- c. Terbutaline 200 mcg/kg twice daily for 4 weeks
- d. Terbutaline 500 mcg/kg twice daily for 4 weeks
- e. Isoproterenol 3/5 mcg/kg twice daily for 4 weeks

One week prior to beginning medications all animals will be immunized with human gamma globulin (HGG). Just prior to beginning the medication blood will be drawn and IgG, IgM, and IgA levels will be measured. Antibody titer to HGG will be determined. On the seventh day of the medication regimen the rats will be given a booster of HGG along with a primary immunization of KLH. After the fourth week of therapy the rats will have blood taken for the determination of immunoglobulin, secondary response to HGG and primary response to KLH. Immunoglobulins will be measured by passive hemagglutination and radial immunodiffusion. Antibodies will be determined by passive hemagglutination.

Progress: A few animals remain to be treated and analyzed in each group. Completion is expected in FY82.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/35 Status: Ongoing

Title:

SWOG 7955: Treatment of Early Squamous Cell Ca of the Head and Neck with Initial Surgery and/or Radiotherapy Followed by Chemotherapy vs No Further Treatment Phase III

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Allergy Clinic Assoc Investigators

Key Words:

Carcinoma, head and neck

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine if the disease-free interval and survival of patients in high risk categories of squamous head and neck cancer can be improved by adjuvant methotrexate after initial surgery, radiotherapy or both have resulted in no clinically evident disease (N.E.D)

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigation Department, WBAMC, and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/36 Status: Ongoing

Title:

SWOG 7902: Combined Modality Therapy with Chemotherapy Radiotherapy and Surgery in Advanced Previously Untreated (Unresectable) Stage III and IV Epidermoid Cancer of the Head and Neck, Phase III

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Oncology

Assoc Investigators

Key Words:

Carcinoma, head and neck

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To compare the survival of Stage III and IV squamous cell carcinoma of the tongue, oral cavity, tonsil, oropharynx, hypopharynx and larynx subjected to radiation therapy followed by surgical excision if possible, versus survival of patients subjected to chemotherapy with Cis-Platinum Oncovin, and Bleomycin (COB), followed by radiation therapy and surgical versus radiotherapy and head and neck surgery.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/37 Status: Ongoing
Title:

SWOG /808: Combination Modality Treatment for Stage III and IV
Hodgkins Disease MOPP 6, Phase III

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Lymphoma; Spermatozoa; Gonad

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

1. To attempt to increase the complete remission rate induced with MOP-BAP alone utilizing involved field radiotherapy in patients with Stage III and IV Hodgkin's disease achieving a PR at the end of six cycles of MOP-BAP.

2. To determine if immunotherapy maintenance with levamisole or consolidation with low dose involved field radiotherapy will produce significantly longer remission duration over a no further treatment group when CR has been induced with six cycles of MOP-BAP in Stages III and IV Hodgkin's disease.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

Two patients have been entered. One has relapsed and the other remains in remission.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/38 Status: Ongoing

Title:

SWOG 7983: Radiation Therapy in Combination w/CCNU in Patients with Incompletely Resected Gliomas of the Brain Grade I and II, Phase III

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Oncology Assoc Investigators

Key Words:

Glioma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

1. The major objective of this study is to compare the survival of patients with incompletely resected Grade I and II gliomas treated with radiation alone versus radiation and CCNU.
2. To compare the effectiveness of radiation therapy versus radiation therapy plus CCNU for remission induction and duration of remission. Because many of these patients will have poorly or non-measureable disease, this will only be a secondary objective.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

One patient has been entered and remains in remission.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/39 Status: Ongoing
Title:

SWOG /985: Combined Modality Treatment for ER-Breast Cancer,
Phase III

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Carcinoma, Breast

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To compare disease-free interval and survival among control group Stage I (and Stage II node negative) breast cancer patients whose tumors are determined to be ER- at the time of mastectomy, versus Stage I (and Stage II node negative) ER- patients treated with adjuvant CMFV for six months.

To document recurrence patterns among untreated patients with Stage I breast cancer whose tumors are determined to be ER- at the time of mastectomy.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/40 Status: Ongoing
Title:

Exercise Induced Asthma in Basic Trainees

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC S.R. Smith, MC

Dept/Sec: Dept Medicine Assoc Investigators
Key Words:

Asthma

Accumulative MEDCASE Est Periodic
Cost \$18,050 OMA Cost: Review Results
Study Objective:

This study is undertaken to determine the incidence of exercise induced asthma in basic trainees. The study will attempt to identify these individuals by pulmonary function testing and the American Thoracic Society questionnaire.

Technical Approach:

Each BCT recruit will fill out an ATS-DLD /8 questionnaire regarding his family, personal and medical history. Standardization of this questionnaire has previously been accomplished. While being held in the reception station, Fort Bliss, each recruit will undergo pulmonary function testing. Those individuals with subtle spirometric abnormalities (i.e. reduced mid and terminal flows) or with a mild obstructive ventilatory defect will undergo exercise testing. For the purpose of this study the grading system devised by the Committee on Pulmonary Physiology, American College of Chest Physicians will be followed. Although extensively used as clinical recommendations, the sensitivity and specificity of the questionnaires and pulmonary function tests are conjectural. Statistical analyses will follow available guidelines. Exercise testing will be carried out on a bicycle ergometer. Exercise workloads will be increased 25 watt seconds each minute. During the last 15 seconds of each minute period, the heart rate, minute ventilation test will be continued until a heart rate of eighty percent of the age adjusted maximum heart rate is attained or until the patient fatigues. During exercise, oxygen saturation will be monitored with an ear oximeter. If oxygen saturation drops below 75 percent, the study will be stopped. Spirographic tracings will be

done at 5, 15 and 25 minutes after cessation of exercise as well as at 10 minutes after inhaled bronchodilators. After basic training all individuals will again complete the ATS-DLD questionnaire. Any individuals with new symptoms will be re-evaluated. Retrospective analysis of preinduction pulmonary functions and questionnaires will be carried out to determine if any single factor predicts exercise induced asthma during basic training. Pulmonary function tests will be compared with the normals established by the VA-Army study.

PROGRESS:

Patient entry has been completed and data analysis is in progress.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/41 Status: Ongoing
Title:

WRAMC /810: Prevention of Gonadal Damage in Men Treated with
Combination Chemotherapy/Radiotherapy for Hodgkins Disease and
non-Hodgkins Lymphomas

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Oncology Svc Assoc Investigators
Key Words:

Lymphoma; Spermatozoa, gonad

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To prevent permanent infertility and alterations in normal sexual
function caused by combination chemotherapy in the treatment of
Hodgkin's disease or non-Hodgkin's lymphoma.
Technical Approach:

The details are lengthy and specified in the original WRAMC
protocol. Duplicates are kept on file in the Dept Clinical
Investigation, WBAMC, and are available upon request.

Progress:

No patients have been entered.

AD-A114 731

WILLIAM BEAUMONT ARMY MEDICAL CENTER EL PASO TX
ANNUAL PROGRESS REPORT, FISCAL YEAR 1981.(U)
SEP 81 L L PENNEY

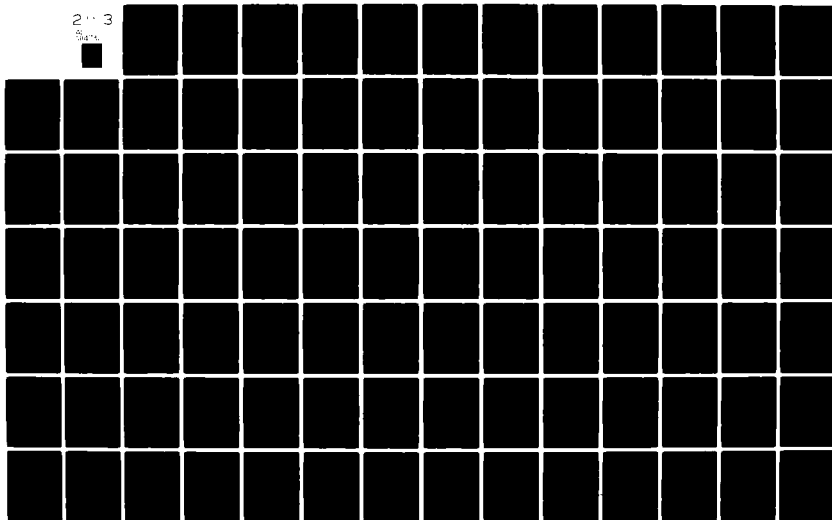
F/G 6/5

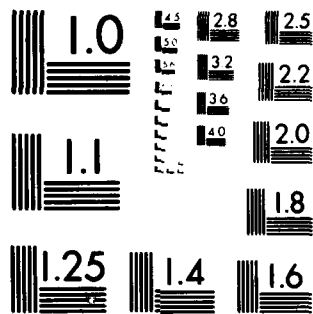
UNCLASSIFIED

NL

203

DATE





MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS 1963-A

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/04 Status: Ongoing
Title:

Can Nuclear Scanning Predict Resolution of Osteomyelitis

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT G. Graham, MC

Dept/Sec: Nuclear Medicine Assoc Investigators
Key Words:

Bone scanning; Osteomyelitis

Accumulative MEDCASE Est Periodic
Cost OMA Cost: \$399(399) Review Results
Study Objective:

To determine the sensitivity of Tc-PyP bone scan to follow the resolution of osteomyelitis under treatment.

Technical Approach:

After anesthetizing rabbits with IV ketamine, right and left rear legs will be surgically prepared. Right and left legs will be randomized, treated and untreated. Control animals will not be the same rabbit as treated rabbit.

The right rear leg will be injected percutaneously through the lateral aspect of the metaphysis of the tibia into the medullary cavity with 0.01 cc of a sclerosing agent (Five percent sodium morrhuate) and a 0.01cc of a suspension of Staphylococcus aureus.

The left rear leg will be injected percutaneously as above and 0.01cc of the sclerosing agent and 0.01cc of normal saline will be instilled.

A technetium scan will be done on both legs at two and four weeks. Concerning the right rear leg, blind readings will be made. The physician reading the scan will not know which leg was used nor whether the animal is treated or untreated.

(1) If the scan remains negative at four weeks, the animal will be sacrificed and the right tibia cultured.

(2) If the scan becomes positive the animal will be treated and scans will be repeated at two week intervals. If the scan becomes

negative the animal will be sacrificed and the tibia cultured. If the scan remains positive beyond eight weeks the animal will be sacrificed and the marrow will be cultured.

Concerning the left rear leg: If the scan remains negative at four weeks, further study will be done of the area. If the scan becomes positive the animal will be sacrificed irregardless of the right leg study, and the left tibia cultured to determine the etiology of the positive scan.

Progress:

With the model described osteomyelitis has been established in the initial animals studied. The mortality is high, but survivors have positive scans. The study is progressing to diagnostic modality and treatment comparisons.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/05 Status: Ongoing
Title:

The Role of Food Allergy in the Pathogenesis of Migraine Headache

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Clinic Assoc Investigators
Key Words:

Food allergy; Migraine headache

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

Assess whether skin testing to a battery of food allergens is of value in defining a diet which will cause a decreased frequency of migraine headaches in affected patients.

Technical Approach:

Subjects will be 18 years or older. They will be selected from the population of the Neurology Clinic, WBAMC. They will be judged by one of the investigators to have migraine syndrome. The nature, the purpose, and proposed benefits of the study will be explained to them. If they are agreeable, the following will be done: (1) Any medications being used for chronic migraine prophylaxis will be discontinued. (2) They will be given a supply of medication for acute migraine attacks. (3) They will report to the Allergy Clinic where the following will be performed:

- a. A history regarding possible food provoked mi.
- b. Prick puncture testing on the back to 15 common foods.
- c. A diet will be prescribed avoiding those foods which are positive on skin testing (2 mm wheal greater than control).
- d. A small blood serum specimen (5 ml) will be collected and frozen for later use if required.

If there are no positive skin tests, the patient will be placed on a corn, egg, milk, wheat free diet. The duration of the diet will be eight weeks. The patients will record symptoms and medications on the diary sheets. Each four weeks the patients will meet with one of the investigators. At the end of eight weeks those who appeared to have had a positive response, that is complete absence of attacks or a greater than 50 percent diminution, will remain on the diet.

Those patients will then undergo a double-blind challenge supervised by one of us. All of the materials for the challenges will be prepared by the other investigator and his staff. The challenge shall be performed in the following manner. Patients will be given a group of opaque capsules containing placebo or freeze-dried foods. The foods chosen will be according to what was eliminated. Interspaced with the foods will be capsules containing placebo (lactose). The maximum amount of challenge food given in one day will be 8 gms. They will take these capsules on a daily basis. This diet challenge period will be individualized for each patient, and may vary in duration. Patients will continue to complete the diary sheets and be seen every four weeks.

Criteria for evaluation of the results will be:

- a. Definitely positive: Significant relief of migraine attacks and positive challenges.
- b. Possible positive response: One of the challenges positive, one negative, diet trial yields relief.
- c. Equivocal placebo effect: Diet trial yields good response in relief of headaches; challenges are negative.
- d. Negative: No relief with the diet trial.

Progress:

Eight patients have been entered and are currently being followed.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/05 Status: Terminated
Title:

Evaluation of Antidiar^R and Lomotil^R in Acute Diarrheas
(Protocol No AD-2-2 Sponsored by Armour Pharmaceutical Co)

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT D. Bohman, MC

Dept/Sec: Dept Medicine Assoc Investigators
Key Words:

Diarrhea

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

Evaluate the effect of Antidiar^R in the treatment of acute diarrhea, compared with treatment by Lomotil^R a reference drug of proven efficacy, and a placebo.

Technical Approach:

Ambulatory individuals, age 18-55, presenting with symptoms compatible with a diagnosis of acute diarrhea will be considered for this study. The diarrhea must have begun less than 48 hours before enrollment in the study, and the patient must have experienced at least three watery, liquid or loose bowel movements within the previous 24 hours. One stool must be collected and inspected by the field investigator to verify its composition.

Criteria for exclusion: Chronic gastrointestinal disorder, including chronic constipation or diarrhea. Any other acute gastrointestinal disorder within the past 30 days. Any other serious concomitant disease. Hyperthyroidism or other systemic cause for diarrhea. Alcoholism. High fever and/or leukocytosis. Use of any antidiarrhea agent (other than the study medication). Concurrent use of any medication vital to the patient's welfare (because of the possibility that the study drug might interfere with its absorption). Inability or unwillingness to comply with the protocol.

Progress:

The principal investigator has been reassigned. No response has been forthcoming from written requests forwarded to his current address.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/08 Status: Ongoing
Title:

Effect of Simultaneous Streptokinase Reperfusion with GlK,
Nifedipine, or Hyaluronidase on Infarct Size in the Canine Heart

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT R.D. Latham, MC

Dept/Sec: Dept Medicine Assoc Investigators
Key Words:

Myocardial infarction; Streptokinase; Nifedipine; Hyaluronidase

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

Determine if the simultaneous administration of GlK or hyaluronidase, or nifedipine with streptokinase results in a significant reduction in infarct size and increased preservation of left ventricular function as compared with reperfusion alone. This protocol will also assess whether the administration of hyaluronidase or nifedipine prior to reperfusion will salvage ischemic myocardium.

Technical Approach:

Twenty large mongrel dogs will be divided into four groups of five dogs each.

- I Streptokinase alone
- II Streptokinase plus GlK
- III Streptokinase plus nifedipine
- IV Streptokinase plus hyaluronidase

Technical Approach:

Five mongrels will be anesthetized with morphine and thipental. A mechanical ventilator will be utilized and ABG'S monitored to ensure adequate oxygenation. Surface lead II EKG and chest lead will be monitored simultaneously. Dogs will not be heparinized.

- a. A pigtail judkins catheter is placed into the left ventricle.
- b. An IV of RL will be maintained at TKO rate.

c. Control EKG on LV pressure curve will be taken. A modified judkins catheter will be utilized to cannulate the proximal LAD artery with placement of a guide wire 0/038. The wire is advanced to the apex, the catheter is removed. A copper coil, prepared in sulfuric acid and rinsed, is advanced several centimeters into the LAD using a straight cut modified judkins catheter.

d. The ECG will be monitored for development of ischemic injury, which will be allowed to remain about two hours.

e. An angiogram will be performed to assess presence of occlusion.

f. A 2F catheter will be advanced to within 1-2 mm of the thrombus.

g. A ventriculogram will be obtained.

h. Perfusion of streptokinase at a rate of 0.3 ml/min or (0.4 ml/min)(5000u/H) will be initiated.

i. Reperfusion is heralded by arrhythmias. VT will be treated by 2-5 mg lidocaine IV bolus via the perfusion catheter. LV pressure will be continuously monitored.

j. An angiogram will be done to assess patency.

k. Infusion will be continued for 30 min.

l. The animal will be heparinized with a dose of 2.0 mg/kg IVP.

m. A ventriculogram will be done to assess EF and wall motion.

n. With catheters removed the animal will remain sedated with SQMS and receive heparin 10,000 units q8 h via heparin lock.

o. After 24 hours the animal will have a repeat angiogram. Monastral blue dye may be injected at this time (optional) 0.5 mg/kg over 30 seconds via a catheter in the left atrium.

p. The animal will be sacrificed using concentrated KCl solution.

q. The heart will be removed and immediately placed in ice cold water to remove excess blood. The myocardium will be cut into no greater than 1 cm slabs. Each section is weighed. A clear glass plate is placed over both sides of each slide and inner and outer margins are traced onto clear acetate with magnifying lens. Areas not perfused by monastral blue dye will also be traced. Then the

slices will be incubated in TTC to delineate the infarction. TTC will be made by combination of Trigma HCl (42.56 gm) Trisma base (16.75 gm) and 2,3,5 triphenyl tetrazolium (20 gm) chloride in 2 liters of distilled water. This will be mixed and stored in the dark. Prior to incubation this solution will be warmed on a hot plate to approximately 37°C. The myocardial slices will be incubated in a pan of the solution (in the dark) for about 20-30 minutes. At least 1 cm of solution covering the slices is needed. A photographic record will be obtained after placing incubated slices in normal saline solution (made by adding 17.8 gm NaCl to 2.5l of ten percent formalin).

r. Incubation in JTC at 37°C will be done.

s. Estimation of infarct size will be measured from the stained myocardium, using a planimeter and plastic transparencies. Differences in weight of infarct/normal myocardium may be compared. The area at risk A_r = ratio of areas not perfused by monastral blue dye to total area of all slices. Area of necrosis A_n = ratio of areas unstained by TTC to total areas of all slices.

GROUP II

Will repeat above procedure with addition of GLK as solvent for streptokinase. GLK will be made by adding 50 units of insulin and 50 mEqKCl/liter D₅W. Nine cc's of this solution plus 1 cc streptokinase 150,000 units/cc to be infused at 0.3 cc/min. (5400 units/hr, which is the same for all groups).

GROUP III

Will undergo same trial as Group I with the addition of nifedipine to the streptokinase solution (to infuse 1 mg/mKg/hr).

GROUP IV

Same trial as above with the addition of bovine hyaluronidase (to deliver 100 units/kg/hr).

Progress:

This protocol was not approved until 8 Oct 81.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/09 Status: Ongoing
 Title:

The Usefulness of Modern Clinical Immunologic Testing in the
 Prediction of Disease, a Pilot Study

Start Date: Est Comp Date:
 Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Clinic Assoc Investigators
 Key Words:

COL L.L. Penney, MC

Accumulative MEDCASE Est Periodic
 Cost \$85,000(Cell Sorter) OMA Cost: Review Results
 Study Objective:

To determine if a one-time global immune evaluation can be used as a
 predictor of future disease.

Technical Approach:

Twenty active duty soldiers will be selected for this study. The
 basis of their selection will be a decision by the Physicians in the
 Troop Medical Clinic that the amount of illnesses of a nontraumatic
 nature, or nonpsychological nature, experienced by this service
 member is greater than expected by his peers. No rigid criteria will
 be established other than the number of visits to the various
 medical facilities. Before the service member is actively entered
 into this pilot study, his records will be reviewed by the principal
 investigator to avoid entrance of an inappropriate subject. The aim
 of this selection process will be to discover twenty patients who
 have well documented histories of a greater than expected frequency
 of infection, either bacterial or viral in nature. After proper
 selection, the subjects will undergo the following immunologic
 studies.

- a. CBC (total white count and differential).
- b. Total serum immunoglobulins (G) (A) (M) (D) (E)
- c. Primary and secondary antibody responses will be measured.
- d. Absolute lymphocyte counts, B and T lymphocyte
 differentiation by rosetting, and surface immunofluorescent
 techniques will be accomplished. Functional lymphocyte activity
 will be determined by response to a lectin, such as PHA; and to an
 antigen, such as SKSD or candida albicans. The supernatant of the
 stimulated culture will be examined for development of lymphokine

activity by evaluation of migration inhibition factor activity. Monocytes/macrophages and polymorphonuclear leukocytes will be evaluated by NBT testing, by chemiluminescence, and by chemotactic ability.

e. In vivo testing will consist of delayed hypersensitivity skin testing performed to a battery of the following antigens:

- (1) Streptokinase
- (2) Streptodornase
- (3) Tetanus toxoid
- (4) C. candida albicans
- (5) PPD
- (6) Trichophyton
- (7) Phytohemagglutinins

All testing results will be compared with normal controls in the laboratory. The results will be evaluated in this light to determine if this type of immune evaluation is able to discriminate between the subject group and usual normal controls.

Progress:

This protocol will be activated when the required equipment arrives and is functional.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/10 Status: Ongoing
Title:

An Evaluation of the Effects of Beta II Adrenergic Agents on Human Immunoglobulins and Antibody Response

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Clinic Assoc Investigators
Key Words:
Beta II agonists; Immunoglobulins LTC S. Smith, MC
LTC M.W. Johnson, MC
CPT I. Weissman, MC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine if the administration of Beta II adrenergic agents affect immunoglobulin levels and the ability to form specific antibodies in the primary and secondary immune response.

Technical Approach:

Forty patients will be selected at random from the Pulmonary Clinic on the basis of a routine therapeutic decision. The physician in charge of their case will judge oral beta II adrenergic agents necessary to improve the patient's clinical pulmonary status. Prior to initiating this therapy, the patients will be told the nature of the study and its importance. The patients will have a blood sample drawn which will be used for analysis. Patients will begin on the appropriate oral beta II adrenergic agent and will return to clinic in one month and have a second specimen of blood obtained.

In those patients in whom it is deemed medically advisable, an influenzal and pneumococcal vaccine immunization will be given. These immunizations will be given only to those patients who may be reasonably expected to benefit from their use. A documented history of previous influenzal immunization will be obtained. The results will be analyzed by comparison of the pre-therapy and post-therapy levels of immunoglobulins. The effects on the expected rise of titer of the secondary antibody response will be compared to normal standards. The titer and presence of the primary antibody response

will be compared to reported standards. The serum specimens collected at both times will be analyzed for the following serum immunoglobulins: IgG, A, M, D and E. In all patients, whether or not they receive immunizations, influenzal and pneumococcal antibody titers will be determined on the pre-therapy and one-month specimens.

Progress:

Fifteen patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/11 Status: Ongoing
Title:

Clinical Evaluation of Tc99m-PIPIDA-Tin as a Hepatobiliary Agent

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC T.J. Brown, MC

Dept/Sec: Nuclear Medicine Assoc Investigators
Key Words:

Hepatobiliary scanning

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

Evaluate the safety and efficacy of Technetium Tc99m PIPIDA-Tin as a hepato-biliary agent.

Technical Approach:

Patients will be 18 years or over, nonpregnant females, non-breast feeding.

Clinical Indications: Patients with history of malignancy to assess metastases or define extent of metastases. Patients with no history of malignancy in whom malignancy is suspected. Liver function determination. Jaundice evaluation. Biliary tract obstruction. Evaluation of acute or chronic cholecystitis. Patients with other medical conditions that, in the investigator's opinion, suggest radioisotope hepato-biliary studies would be useful.

Evaluation of Scan Image: Evaluation of the image quality should be based on the following standards: Good quality image, diagnostically useful - acceptable.

Poor image quality, diagnostically not useful - unacceptable.

Criteria by which efficacy will be evaluated: Comparison with radiographic findings when indicated and available. Correlation with surgery, biopsy, and autopsy findings when available.

Utility of the study: Initial clinical impression should be compared with the final or clinical diagnosis and the utility of the procedure assessed.

Progress:

Forty-three patients were entered in FY81. No untoward or adverse effects have been noted. Image quality and diagnostic capability appear to be excellent with this agent.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/12 Status: Ongoing
Title:

A Novel Method of Hyposensitization Therapy with Russian Thistle Antigen

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Clinic Assoc Investigators
Key Words:

Hyposensitization; Russian thistle antigen

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine if oral administration of Russian Thistle pollen in a pharmacologically modified release form will be capable of: (a) Demonstrating immunologic changes that are comparable to standard parenteral allergen immunotherapy. (b) Demonstrating in a physiologic test, such as nasal provocation, evidence of lessened reactivity to allergen.

Technical Approach:

Thirty adult allergic patients, who are significantly sensitive to Russian Thistle allergen by history and skin testing, will be the subjects for this protocol. The nature and purpose of this study will be explained to them. The study will be conducted from December to March, when ambient Russian Thistle pollen is not present in El Paso.

The subjects will report to the Allergy Clinic. Prior to the initiation of therapy, the subjects will have:

- a. Titrated prick-puncture skin tests performed (3mm wheal end point).
- b. 5 ml blood taken to measure specific serum IgG, IgM and IgE antibodies to Russian Thistle allergen.
- c. Nasal sensitivity to Russian Thistle allergen determined by nasal provocation (doubling of nasal airway resistance as end point).

The patients will be given capsules containing specifically prepared Russian Thistle allergen. This material will be lacquered to avoid digestion and dissolution in the acid media of the stomach. The schedule on a daily basis: 0.15, 0.30, 0.60, 0.90, 1.20, 1.60, 1.90, 2.0, 2.5, 3.0, 4.0, 5.0, 7.0, 9.0, 12.0, 15.0, 20.0, 25.0, 30.0, 40.0, 50.0 mg.

50 mg will be given weekly as a maintenance dose for four more weeks. After this total schedule, the measurements made prior to therapy will be repeated. The results will be analyzed by paired "t" testing of the mean responses.

Progress:

This study has not been activated as it is pending final approval.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/13 Status: Ongoing
Title:

Effect of Streptokinase on the Sinoatrial Node, the Atrioventricular Node, and the Myocardium of the Canine Heart

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT R.D. Latham, MC
Dept/Sec: Dept Medicine Assoc Investigators
Key Words:

Streptokinase; Sinoatrial node; Atrioventricular node

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

Determine if the systemic effects of streptokinase are evident when the drug is administered by intracoronary technique and the effect if any of streptokinase on the SA, AV nodes or myocardium.

Technical Approach:

Approximately ten mongrel dogs will be weighed and anesthetized with pentobarbital using 30 mg/kg dose. The animal will then be intubated with an endotracheal tube and ventilated with approximately 225 cc TV and rate of 14-16 with monitoring of ABG's. A surface lead EKG lead II will be placed. The dogs will be heparinized with dose of 2 mg/kg. Central aortic pressure will be monitored via a catheter placed from the carotid. A median sternal splitting incision will be performed, the heart exposed and cradled in the pericardium. Student's paired t-test will be used to determine the significance between similar observed and control variables. Grouping will be optional depending on initial results.

Progress:

The catheterization techniques have been perfected in pilot animals. Study animals will be entered in FY82.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/15 Status: Terminated

Title:

SWOG /81/: Treatment of Advanced Germ Cell Neoplasms of the Testis: Remission Induction with Vinblastine Bleomycin with Low Dose or High Dose Cis-Platinum

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Carcinoma, testis

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

1. To determine in a randomized fashion the effectiveness of cis-diaminedichloroplatinum (DDP) given in the conventional low-dose schedule daily x 5 days versus high-dose intermittent treatment in remission induction of disseminated testicular cancer, when combined with vinblastine and bleomycin.

2. To determine the survival of patients who achieve a partial remission and are rendered disease-free by surgical removal of residual disease and maintained on the same chemotherapy as patients who achieved complete remission status on chemotherapy alone.

3. To determine the effectiveness of cyclophosphamide, actinomycin-D, Adriamycin and Vinblastine, in the maintenance of remission status.

4. To document the nature and extent of the hematologic and nonhematologic side effects of the various drug combinations.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

No patients were entered. This protocol has been closed by SWOG.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/16 Status: Terminated

Title:

SWOG 7925: Chemoimmunotherapy in Stages III and IV Ovarian Carcinoma: A-C plus BCG, vs. A-C plus Cis-Platinum vs. A-C plus Cis-Platinum plus BCG, Phase III

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Carcinoma, ovarian

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

1. To compare the effectiveness of the SWOG Study, SWOG 7524 best therapy arm - A-C + BCG, vs. A-C + Cis-Platinum for remission induction and/or maintenance of disease-free status and prolongation of survival duration in patients with Stages III and IV ovarian carcinoma (measurable and nonmeasurable disease).

2. To compare the effectiveness of A-C + Cis-Platinum vs. A-C + Cis-Platinum + BCG for remission induction and/or maintenance of disease-free status and prolongation of survival in patients with Stage III and IV ovarian carcinoma (measurable and nonmeasurable disease).

3. To compare the effectiveness of A-C + BCG vs. A-C + Cis-Platinum + BCG for remission induction and/or maintenance of disease-free status and prolongation of survival duration in patients with Stages III and IV ovarian carcinoma (measurable and nonmeasurable disease).

4. To compare the toxicities of the A-C + BCG; A-C + Cis-Platinum and A-C + Cis-Platinum + BCG regimens.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

No patients were entered. This protocol has been closed.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/17 Status: Ongoing

Title:

SWOG /984: The Treatment of Chronic Stage CML with Pulse, Intermittent Busulfan Therapy with or without Oral Vitamin-A, Phase III

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Leukemia

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine the efficacy of standard pulse, intermittent busulfan therapy plus oral vitamin A in prolonging the chronic phase of CML, and hence in prolonging survival.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/18 Status: Ongoing

Title:

SWOG 8001: Evaluation of Two Maintenance Regimens in the Treatment of Acute Lymphoblastic Leukemia in Adults, Phase III

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Leukemia

Accumulative MEDCARE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

1. To evaluate the effectiveness, as determined by the complete remission-rate, of the L10 protocol using Vincristine, Prednisone, and Adriamycin for induction, followed by intensive consolidation in the treatment of adult ALL in a group-wide study.
2. To compare the effect on remission duration and survival of two maintenance regimens: The L10 "eradication" regimen vs. cyclic therapy with POMP-COAP-OPAL.
3. To determine the reproducibility of the FAB histologic classification and correlation to response to therapy of ALL in adults.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

One patient has been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/19 Status: Ongoing

Title:

SWOG 8006: Preoperative Reductive Chemotherapy for Stage III or IV Operable Epidermoid Carcinoma of the Oral Cavity, Oropharynx, or Larynx, Phase III

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology Assoc Investigators

Key Words:

Carcinoma, larynx; Carcinoma, pharynx

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
---------------------------	---------------	-------------------------

Study Objective:

The purpose of this study is to determine the length of remission, recurrence-rates, survival-rates, and pattern of recurrence for patients receiving therapy utilizing surgery and post-operative radiation vs. combined therapy utilizing pre-operative radiation vs. combined therapy utilizing pre-operative chemotherapy, surgery and post-operative radiation therapy in operable Stage III or IV epidermoid carcinoma of the head and neck.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/20 Status: Ongoing
Title:
SWOG 8014: Colchicine in Refractory Chronic Lymphocytic Leukemia,
Phase I-II

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology Assoc Investigators
Key Words:

Leukemia; Colchicine

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

1. To determine the maximum dose of colchicine that may safely be administered on a once weekly basis.
2. To determine the response rate (standard error +/- ten percent) in patients with chronic lymphocytic leukemia.
3. To determine quantitative and qualitative toxicity of the drug colchicine administered on a once weekly schedule.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/21 Status: Ongoing

Title:

SWOG 8012: Treatment for Advanced Adenocarcinoma and Large Cell Carcinoma of the Lung: FOMi vs CPA vs FOMi/CAP, Phase III

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology Assoc Investigators

Key Words:

Carcinoma, lung

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
---------------------------	---------------	-------------------------

Study Objective:

1. To evaluate by pairwise comparison the response-rate, duration of response and survival of 3 regimens FOMi, CPA and FOMi/CAP in patients with advanced (TMN Stage III M1) adenocarcinoma and large cell undifferentiated carcinoma of the lung.
2. To evaluate the degree of non-cross resistance of FOMi in CAP failures and of CAP on FOMi failures.
3. To compare the toxicities and side effects of FOMi and CAP.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/22 Status: Ongoing

Title:

SWOG 8015: Evaluation of Two Combination Chemotherapy Programs, Adriamycin and Cis-Platinum (AP) versus Adriamycin, Cis-Platinum plus VP 16 (VAP), in the Treatment of Extensive Squamous Cell Carcinoma of the Lung, Phase III

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Carcinoma, lung

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

1. To determine the activity, in terms of response rate, remission duration, and survival in patients with extensive squamous cell (epidermoid) carcinoma of the lung, for two combination chemotherapy programs; adriamycin and Cis-Platinum (AP) versus VP 16-213, Adriamycin and Cis-platinum (VAP).
2. To evaluate the relative toxicities of these respective regimens.
3. To assess the feasibility and reliance of applying "measurable versus evaluable" criteria of tumor regression in determining therapeutical response.
4. To correlate tumor grade with response and survival.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/23 Status: Ongoing

Title:

SWOG 8027: The Natural History of Pathological Stage T₁₋₂ N₀
M₀ ER + Breast Cancer, Phase III

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.C. Farley, MC

Dept/Sec: Dept Medicine, Oncology

Assoc Investigators

Key Words:

Carcinoma, breast

Accumulative MEDCASE
Cost

Est
OMA Cost: \$1898(1898)

Periodic
Review Results

Study Objective:

To document recurrence rates, patterns of recurrence, and survival among patients with Stage I or Stage II node negative (T₁₋₂ N₀ M₀) breast cancer whose tumors are determined to be estrogen receptor positive at the time of surgery.

Technical Approach:

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Dept Clinical Investigation, WBAMC, and are available upon request.

Progress:

No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/24 Status: Ongoing

Title:

The Re-Use of Hollow Fiber Hemodialyzer, a Randomized Trial

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ M. Siedlecki, MC

Dept/Sec: Dept Medicine, Renal Cl

Assoc Investigators

Key Words:

Hemodialysis

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

A double blind, randomized cross-over study of the effect of hollow fiber artificial kidney re-use on chronic hemodialysis patients.

Technical Approach:

In a double blind fashion, 2 groups, new and re-used group, 5 patients each will be treated concurrently with new and re-used hemodialyzers. In the re-used group each patient will be treated with the same "own" kidney; the kidneys will not be mixed. The hemodialysis procedure will not be changed in any way from the way it is practiced now. The rinsed hemodialysers will be used six times and after clearance determinations, done during the 5th re-use, discarded.

Progress:

Patient entry has begun. Twelve to 18 months will be required to access the necessary sample size.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/28 Status: Ongoing

Title:
The Effects of Erythromycin Treatment on Neutrophil Chemotaxis

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy Cl Assoc Investigators

Key Words:

Chemotaxis; erythromycin

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
------------------------------	------------------	----------------------------

Study Objective:

To determine if in vivo treatment with erythromycin leads to an improvement in neutrophil chemotaxis in vitro.

Technical Approach:

Twenty adult patients with severe atopic dermatitis will be selected from patients attending the Dermatology Clinic. The nature and purpose of the study will be explained to them. Diagnostic criteria for atopic dermatitis will be the usual clinical criteria for atopic dermatitis to include: (1) Family history of atopy. (2) characteristic distributions of lesion. (3) white dermatographism. (4) characteristic scaly lichenified, or nummular appearance. (5) Elevated serum IgE level. (6) No evidence of contact dermatitis. (7) Biopsy compatible with atopic dermatitis. The skin manifestations must be present, along with two or three other characteristics. The twenty patients will have atopic dermatitis that has not responded to topical corticosteroids. They will be divided randomly into two groups, one to receive erythromycin, 250mg, QID; one to receive 10mg prednisone TID for five days, and 30mg QOD in a.m. for five further doses. A third group of 10 patients treated only with Eucerin and antihistamines of the H₁ class will be studied as controls. Blood samples will be obtained just prior to beginning and at the end of the medication course. These samples will be used to provide white cells (polymorphonuclear leukocytes) for chemotaxis in a modified Boyden

Chamber technique, and an agarose technique. Random migration and the response to various chemoattractants will be measured. The results of the pre-therapy and post-therapy specimens will be compared. The differences in changes between groups will also be compared and if the results suggest an effect from the erythromycin beyond the effect from the prednisone, the study will be expanded.

Progress:

This study will be activated when the appropriate technical support is available.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/29 Status: Ongoing

Title:

The Effect of a Lipoxygenase Inhibitor on Phytohemagglutinin Stimulated Lymphocyte Blastogenesis in Rheumatoid Arthritis.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy C1

Assoc Investigators

Key Words:

Lipoxygenase; Rheumatoid arthritis; lymphocyte stimulation

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$1055(1055)

Review Results

Study Objective:

To determine effects of a lipoxygenase inhibitor on lymphoblastogenesis in patients with rheumatoid arthritis.

Technical Approach:

Ten patients with active rheumatoid arthritis will be chosen from the Rheumatology Clinic. Five normal volunteers will be selected from among the physician staff of WBAMC. Thirty milliliters of blood will be drawn from each subject and lymphocytes separated for microtechnique phytohemagglutinin lymphocyte stimulation. The cultures will be done in the usual fashion and also with the addition of four concentrations of 5,8,11 eicosatrienoic acid (2×10^{-7} , 10^{-5} , 10^{-5} , 10^{-4} molar). The response of the normal and rheumatoid cells to this compound, as contrasted to the usual cultures, will be compared.

Progress:

Patients will be entered when appropriate technical support is available. Preliminary work to establish experience with the technique has been accomplished.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/30 Status: Ongoing

Title:

The Effects of a Histamine (H₂) Antagonist on the Lupus-like Syndrome of New Zealand Mice

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy C1

Assoc Investigators

Key Words:

Cimetidine; Lupul erythromatosis

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine if routine treatment with an H₂-receptor antagonist will influence the time course or severity of the systemic lupus erythematosus-like syndrome of New Zealand mice.

Technical Approach:

One hundred fifty NZB/NZW female mice will be used for this experiment. At the beginning of the experiment they will be approximately one month of age. One-hundred mice will be the treatment group; 50 mice will be the sham group. Five out of seven days the treated mice will receive an injection of 100 mg/kg cimetidine. The control mice will receive an injection of vehicle. Beginning at three months of age, ten treated mice and five sham mice will be sacrificed. Blood will be obtained and analyzed for autoantibodies and immune complexes. The kidneys will be processed by florescent staining for immunoglobulins and complement. Any mouse that dies spontaneously will be counted in the appropriate group for that month and an attempt to utilize the kidney for immunofluorescence will be made.

Progress:

This protocol has not been activated.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/36 Status: Ongoing

Title:

Phase II Studies on Ketoconazole (Keto) - Comparison of Two Different Doses of Keto in Treating Coccidiomycosis

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT Idelle Weismann, MC

Dept/Sec: Dept Medicine

Assoc Investigators

Key Words:

Coccidiomycosis; Ketoconazole

MAJ S. Smith, MC

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine the most efficacious dose of Keto for humans with coccidioidomycosis. To evaluate the toxicity of Keto in humans with doses up to 1500 mg per day. To evaluate the CSF penetration of very high doses of Keto.

Technical Approach:

The details are lengthy and specified in the original protocol, which is on file in the Dept Clinical Investigation, WBAMC, and is available upon request.

Progress:

This IND protocol had not received final approval from HSRRB at the close of FY81.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/38 Status: Ongoing

Title:

The Development of Subsensitvity to Atropine

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy C1

Assoc Investigators

Key Words:

Atropine; Asthma

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine if repeated use of atropine sulfate as a bronchodilator, by the inhalant routes, leads to development of subsensitvity.

Technical Approach:

Twenty adult asthmatic patients will be selected at random from the Pulmonary and Allergy Clinics at WBAMC. The nature and purpose of the study will be explained. On the first day of the experiment they will be tested at the Pulmonary Function Lab according to the following protocol:

- a. 24 hours without oral bronchodilators
- b. Baseline pulmonary functions consisting of conventional spirometry, flow volume loops, and plethysmography.
- c. Inhalation of atropine sulfate 2 mg by nebulizer.
- d. Repeat pulmonary function.

After this the patients will be instructed in the use of a home nebulizer. They will use atropine sulfate 2 mg by nebulizer three times a day for 14 days. At the end of the period, the patients will undergo the same testing as on the initial day. If there is a decrease in response, then ten subjects will be retested after inhalation of 0.5 mg atropine and ten after inhaling 1.0 mg atropine, in addition to the previous 2.0 mg.

Analysis will consist of t-testing of the mean response on each occasion. In the ten subjects of each incremental group, comparison will be made to ascertain which increment, if one is required, to restore responsiveness to the original testing level.

Progress:

The study will be activated when appropriate technical support is available.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/39 Status: Ongoing
Title:

The Usefulness of NonAcetylated Salicylates in the Treatment of Inflammatory Disease in Patients with Aspirin Idiosyncratic Asthma.

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy CI Assoc Investigators
Key Words:

Salicylates; Asthma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine if non-acetylated salicylates can be used safely in the treatment of aspirin-idiosyncratic asthmatics with inflammatory disease.

Technical Approach:

Thirty patients with a history of aspirin idiosyncrasy will be selected from the Pulmonary and Allergy Clinics of WBAMC. The nature and purpose of the study will be explained to them. They will report to the Pulmonary Function Lab on four occasions. They will be tested according to following protocols. Measured pulmonary functions will be conventional spirometry and flow volume determinations on each occasion.

DAY 1	Day 2	Day 3	Day 4
Placebo	Aspirin	Disalcid	Trisilate
1 cap	32 mg	250 mg	250 mg
2 cap	64 mg	500 mg	500 mg
3 cap	128 mg	750 mg	750 mg
4 cap	325 mg	1000 mg	1000 mg

The patients will not take oral bronchodilators for 24 hours except for corticosteroids. They will be managed by inhaled bronchodilating agents. Each dose will be spaced 30 minutes apart. All medications will be given in identical opaque white capsules, and the patient will be blinded as to the contents of these capsules.

A significant test for each person will be a fall in one second forced expiratory volume greater than twenty percent of predicted FEV₁, over the fall during the placebo challenge. Any patient who develops clinical symptoms will have their bronchoconstriction reversed. Any subject whose aspirin challenge is negative will be excluded from the study. Each testing will be compared to the placebo day, in terms of possible positive responses.

Specifically, patients will not be entered unless their FEV₁ is greater than eighty percent of predicted at the onset of the study, and patients who develop greater than a twenty percent fall in FEV₁ will be eliminated from the study at that point.

Progress:

Patient entry should commence in FY82.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/40 Status: Ongoing

Title:

The Usage of Beta 2 Agonist in Topical Treatment of Allergic Skin Reactions.

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy Clinic Assoc Investigators

Key Words:

Beta II agonist; Histamine; Eosinophil migration; Mast cells

Accumulative MEDCASE	Est	Periodic
Cost \$8,037	OMA Cost: \$825(825	Review Results

Study Objective:

To determine whether locally applied B₂ agonist suppresses the histamine release, eosinophil migration response, and ultrastructural changes of mast cell in human allergic skin reactions.

Technical Approach:

Adult patients will be selected on the basis of a 4+ positive prick skin test to ragweed allergen from the Allergy Clinic. They will undergo skin blister provocation and skin biopsy and the resultant materials tested.

Progress:

Fifty subjects have volunteered for this study. Data accrual has been rapid and completion is anticipated in FY82.

Detail Summary Sheet

Date: 1 Oct 81	Prot No: 81/45	Status: Ongoing
Title: The Effects of Chronic Bronchoconstriction on Bronchial Smooth Muscle and Bronchial Architecture		
Start Date:	Est Comp Date:	
Principal Investigator:	Facility:	
LTC L.E. Mansfield, MC		
Dept/Sec: Dept Medicine, Allergy Clinic	Assoc Investigators	
Key Words:	P.A. Miles, MD., DAC B.E.F. Reimann, DSc, DAC	
Bronchoconstriction		
Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost: \$338(338)	Review Results
Study Objective:		

To determine if repeated bronchoconstriction caused by immunologic or chemical stimulus leads to the observed bronchial smooth muscle hypertrophy and the other changes noted in the pathological examination of the asthmatic lung.

Technical Approach:

Weanling guinea pigs will be used for this study. They will be divided into four groups of ten animals each, according to the protocol below.

Group I: Saline challenge, no bronchoconstriction expected.

Group II: Will be challenged daily until wheezing with 48/80, 1 mg per ml, by inhalation.

Group III: Guinea pigs who have been sensitized to egg albumin, induced with pertussis vaccine, will comprise this group. They will undergo inhalation challenge with a 1:100 w/v egg albumin solution until wheezing.

Group IV: As in group III, with prior inhalation of 20 mg cromolyn, before being challenged with egg albumin.

This procedure will be carried out five days per week for a period of twelve weeks. This will approximate the time in a human life span from childhood until sexual maturity.

A lucite chamber will constrain the guinea pigs during respiratory function studies for aerosol administration. The end point of a challenge will be wheezing in a guinea pig, which can be heard audibly through a stethoscope and can be monitored by nasal and perioral cyanosis. At the completion of the study, each of the animals will be sacrificed and a wet and dry weight of the lung obtained. The pulmonary tissue will be submitted for routine histological examination. Specimens will be randomized and blinded.

The following data will be evaluated:

- a. Differences in the weight of the lung between the four groups.
- b. Microscopic examination of lung tissue containing bronchi, and a second examination containing bronchials. During this examination, thickness of the bronchial smooth muscle, the basement membrane, and any evidence of bronchial mucous gland hyperplasia will be evaluated.
- c. If there are any significant changes found under light microscopy, selected segments, which have been prepared from the control group, and the three challenge groups will be examined under electron microscopy. It would be hoped that this examination may provide further light on distortions of the bronchial architecture.

Progress:

This protocol was activated at the close of FY81. Progress will be detailed in the FY82 report.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/54 Status: Ongoing

Title:

High Resolution Electrophoretic Screening of Body Fluid Proteins

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT I.L. Levey, MC

Dept/Sec: Dept Medicine

Assoc Investigators

Key Words:

Electrophoresis

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$883(883)

Review Results

Study Objective:

Study the qualitative and quantitative patterns of proteins in human serum by high resolution two-dimensional electrophoresis. Proteins will be separated in the first dimension according to the net electrical charge of their constituent amino acids by the technique of isoelectric focusing, and in the second dimension according to their molecular weight by electrophoresis in the presence of sodium dodecyl sulfate. This technique can resolve, in theory as well as in practice, a thousand or more individual peptides. Under appropriate conditions, this technique can be expected to depict many of the individual protein components in human serum and other body fluids. If such resolution can be achieved, and a very large number of different peptides be seen, then variations related to disease may be studied, identifications made and the entities of greatest interest isolated.

While the spectrum of serum components in both health as well as disease is of interest, initial studies will be directed toward patients (1) with malignant disease (2) those undergoing chronic hemodialysis, (3) those with hepatic disease, and (4) those with inflammatory/autoimmune disease.

Technical Approach:

The major objective of the proposed research is to analyze the protein composition of human serum in health and disease. Four specific categories of patients have been selected for initial screening based upon either well-documented abnormalities of routine serum protein electrophoresis or their potential for protein abnormality. These categories include:

a. Patients with malignant disease, including plasma dyscrasias. Alterations of both beta and gamma globulins have been noted, as well as microheterogeneities of serum albumin. Patients will be studied before and during therapy, as well as during progression of disease.

b. Patients with protein-losing nephropathies and those undergoing hemodialysis. Many patients on hemodialysis develop protein electrophorograms resembling type 3 hyperlipoproteinemia. Additionally, those with collagen vascular diseases often experience remission of symptoms and occasionally alteration of serologic status following dialysis.

c. Patients with hepatic disease. The liver is the primary organ for synthesis of most plasma proteins other than the immunoglobulins. However, the Kupffer cells of the liver are involved with the immune system in that they process antigens absorbed from the gut. As a consequence, disorders involving the liver can result in abnormalities of virtually all of the plasma proteins.

d. Patients with inflammatory and/or autoimmune disease. Patients with rheumatic diseases frequently demonstrate plasma protein abnormalities, most commonly associated with the inflammatory response and those resulting from increased antigenic stimulation of the immune system.

Patients will be selected from those with documented abnormalities of routine serum protein electrophoresis as well as those encountered during routine ward activities.

Progress:

The principal investigator has arranged research time in January 1982 to begin this study.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/55 Status: Ongoing

Title:
Ticlopidine Hydrochloride - A Clinical Trial in Patients with
Transient Cerebral or Monocular Ischemic Attacks

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL M. Maccario, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:
Ticlopidine; cerebral
ischemia

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine in a double-blind, randomized, parallel, controlled clinical trial whether ticlopidine hydrochloride can prevent the occurrence of transient or prolonged retinal or cerebral ischemic attacks (CIA), cerebral infarction (CI) as well as occlusive cardiovascular events in patients who are suffering from TIA or amaurosis fugax.

Technical Approach:

Only nonsurgical candidates, or surgical candidates refusing surgical therapy, will be considered eligible for inclusion in this trial. Each qualified subject (to be verified by a neurologically qualified referee) will be randomly allocated to either ticlopidine hydrochloride or identical appearing control medication and in a double-blind fashion. Each participating center will have a separate randomization code for their institution and will essentially operate independent of other institutions enrolled in this trial. All data and case report forms generated by the participating centers will be forwarded to the central data processing center for inspection, handling, coding, correction, etc. Interim planned evaluations of accumulated data will be undertaken to monitor the safety and efficacy of the medications. Any proven or unacceptable side effects or toxicity due to therapy, or any obvious or sustained lack of efficacy of ticlopidine hydrochloride would be reason for premature termination of this clinical trial.

These properties of maintained prostacyclin production by the vessel wall and lack of platelet responsivity to prostaglandin endoperoxide stimulation in ticlopidine hydrochloride treated animals may be two very important therapeutic advantages of ticlopidine hydrochloride over ASA and the other non-steroidal anti-inflammatory compounds.

Ticlopidine hydrochloride at the dose of 250 mg BID for this therapeutic trial is well tolerated and safe in clinical tolerance and therapeutic studies conducted in the USA, Europe, and Japan. We anticipate no intolerance with the possible exception of infrequent, mild initial gastrointestinal discomfort in some patients. A more extensive description of ticlopidine hydrochloride is to be found in the drug monograph.

Purpose of Trial: The short term goal of this study is to investigate the effect of ticlopidine hydrochloride vs controlled therapy (ASA, or placebo) in preventing or reducing the incidence of CIA and/or amaurosis fugax attacks.

Progress:

This IND protocol is awaiting final approval by HSRRB.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/57 Status: Ongoing

Title:
Late Incidence of Chronic and Occult Constrictive Pericardial
Disease in Patients Treated by Radiotherapy for Hodgkins Disease

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL M. Maccario, MC

Dept/Sec: Dept of Medicine Assoc Investigators

Key Words:

Hodgkin's Disease; Radiotherapy; Pericarditis

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost:	Review Results
Study Objective:		

To determine the incidence of pericardial disease in patients 24 months or greater post-radiotherapy for Hodgkin's Disease.

Technical Approach:

Thorough history and physical examination as well as blood studies, chest-x-ray and EKG will be performed. Ultrasound studies will be performed on the heart as well as MUGA scans to record the activity of the heart. Swan-Ganz cateterization will be performed in the Cardiac Cath Lab under the supervision of staff cardiologists, injecting novocaine at the elbow for anesthesia. With the aid of fluoroscopy, the catheter will be advanced through the heart into the arteries to the lungs. The catheter will allow measurement of pressures in the heart, requiring about 45-60 minutes.

Progress:

This protocol was approved late in FY81. No patients have been entered.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/58 Status: Ongoing

Title:
The Prevalence of Antibiotic Tolerant Staphylococcus Aureus in
Nasal Cultures of Different Adult Population Group

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ Frank J Baker, MC

Dept/Sec: Dept Medicine, Infect Dis Assoc Investigators
Key Words:

Staphylococcus

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To perform an epidemiological survey of Staphylococcus aureus tolerance from isolates not causing clinical infection and determine prevalence rates in different adult population groups.

Technical Approach:

Three population groups consisting of 100 individuals in each group will be studied.

Normals consisting of two subpopulations. Young adults consisting of a defined population, i.e., active duty personnel billeted on post. Older adults consisting of a defined population, i.e., personnel in Health Services Command. This group would be composed of individuals free of chronic disease on no medication or antibiotic therapy.

Outpatients on antibiotics. Young adults from the Dermatology Acne Clinic. Older adults from the Pulmonary Clinic, patients with chronic obstructive pulmonary disease on cyclical antibiotic therapy.

Population with a high prevalence of staph nasal carriage. Renal dialysis and insulin dependent diabetic patients. Hospital personnel. Nasal swabs with culturettes will be obtained from each individual.

(1) All nasal swabs will be streaked on sheep blood agar (SBA). Identification of staph aureus will be by standard methods as per the Manual of Clinical Microbiology, i.e., colonial morphology gram stain.

(2) MIC will be performed in duplicate by standard methods as per the Manual of Clinical Microbiology. After primary inoculation and identification of an organism as staph aureus:

(a) A log phase, four hour growth of the organism will be prepared in Mueller-Hinton Broth (MHB). The inoculum will be standardized to a 0.5 McFarland and a 1/200 dilution prepared. Colony counts will be performed on each inoculum with a desired final concentration 1 or 2×10^5 organisms/ml

Conclusions: If the prevalence rates were significantly different among the study population groups, the contribution of various epidemiological factors could be determined. If the prevalence rates of tolerant organisms were less than those causing clinical infection, the question of increased virulence and microbiological change of the organism from a colonizer to an invasive form would be raised. Conversely, if the prevalence was equal to or greater than those causing clinical infection, the clinical importance might be lessened for this phenomenon.

If in subsequent studies tolerance was found to be therapeutically important, i.e., necessitating higher dosages or different antibiotics not standardly used for staphylococcal infections, this prior identification of epidemiologic factors might aid in initial selection pending further characterization of the organism. By having identified those individuals with high prevalence rates of tolerant organisms and at increased risks for clinical infections with those organisms empiric selection of treatment might be facilitated.

Progress:

This late FY81 protocol has not been started.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/54 Status: Ongoing

Title:

A Comparison of Streptokinase/Streptodornase (SK/SD) with Streptokinase (SK) alone in Delayed Hypersensitivity Skin Testing of Children Ages 5-17.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy Cl

Assoc Investigators

Key Words:

Streptokinase; Streptodornase; Delayed hypersensitivity

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine if streptokinase alone can replace streptokinase/streptodornase in the in vivo evaluation of cell mediated immunity by delayed hypersensitivity skin testing in children. To also evaluate the effects of acute minor illness on these skin tests.

Technical Approach:

One hundred normal children, ages 5-17 years, approximately 50 females and 50 males, attending the Pediatric Clinic for routine school physicals, will be entered in a sequential order. They will be free of illnesses. The nature and purpose of this study and its possible risks will be explained to them and their parent(s). Two skin test sites will be selected, one on the right volar aspect of the forearm, the second in a similar location on the left forearm. SK/SD and SK sites will be alternated from left to right in an even/odd rotating sequence. The children will receive 0.1 ml of extract containing 100 u SK/25u SD intradermally in one site and 0.1 ml extract containing 100u SK intradermally in the second site.

A second study group will consist of children 5-17 years of age attending the Pediatric Clinic for minor infectious illness, usually upper respiratory infection.

The tests will be read at 24 and 48 hours. A positive response will be 5mm or greater of induration. However, all responses will be measured and recorded.

The results will be analyzed by nonparametric (Wilcoxon's signed rank test) and parametric (paired t-testing) analysis. The frequency of positive tests in the non-ill and ill groups will be compared by t-testing and the fifty percent probability test. Other evaluations will be performed as deemed appropriate by the statistical consultant.

Progress:

Fifteen subjects have been studied. Patient entry should be complete by March 1982.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/55 Status: Ongoing

Title:

Utility of Furosemide in Early Oliguric Renal Failure. Part of a Multi-center study.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ S.F. Gouge, MC

Dept/Sec: Dept Medicine

Assoc Investigators

Key Words:

Furosemide; Renal failure

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

A randomized study of furosemide effect on the outcome of oliguric acute renal failure. Can this diuretic convert a patient with oliguric acute renal failure to non-oliguric acute renal failure

Technical Approach:

Patients with renal oliguria will be considered for this study. Non-oliguric patients will also be included. However, the patients should not have post-renal obstruction, and if obstruction is suspected on clinical grounds, a complete workup will be done. In addition, pre-renal factors contributing to the renal failure, such as hypotension, volume depletion and congestive heart failure, will be corrected. Any patient with diminished hearing as determined clinically by questioning will be excluded from the study. Also any patient that experiences transient hearing loss after the first furosemide dose will be excluded from subsequent dos.s. Absence of administration of furosemide or other diuretic agents within the previous twelve hours will be a criteria for entry as will serum creatinine greater than 2.0 mg/dl.

There will be two patient groups, furosemide and saline placebo, as determined by the use of a random numbers table. Consecutive patients assigned an even number from the random numbers table will receive furosemide. Patients assigned an odd number will receive saline. The random numbers table will be employed by using horizontal rows.

Progress:

Patient entry has just started on this newly approved protocol.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/27 Status: Ongoing

Title:

Effect of Reassessment on Deterioration of Diabetic Patients' Knowledge and Management Skills, and on Compliance.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ J.R. Bonnell, ANC

Dept/Sec: Dept Nursing

Assoc Investigators

Key Words:

Diabetes mellitus

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine if frequent reassessment at one month, three months, six months intervals improves diabetic patients' knowledge and management skills and compliance.

Technical Approach:

Two groups of adult diabetic patients, ages 18-70, will be randomly selected from the total diabetic population of a large military medical center, and assigned randomly to either a control group or an experimental group. Both groups will be given identical instruction on diabetic management skills and diabetic information. The checklists will be maintained in a file and updated appropriately.

Patients in both groups will need to have correct performance of at least five objectives one week after the initial teaching has been done in order to qualify for entry into the study. Patients in the experimental group will require reassessment at one month, three months, and six months intervals. Patients in the control group will require reassessment at six month intervals, with no intervening assessment. Additional factors that will be collected include: age, duration of diabetes, previous attendance at formal diabetes teaching sessions such as classes.

Progress:

Patient accrual is nearing completion. Followup of study patients will be complete in the second or third quarter of FY82 and a thesis will be prepared from the data.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/50 Status: Completed

Title:

Oxygenation and Subarachnoid Block Regional Anesthesia

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT B.A. Aubin, ANC

Dept/Sec: Dept of Nursing

Assoc Investigators

Key Words:

Subarachnoid block

CPT Cheryl Murphy, ANC

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine in patients undergoing subarachnoid block (SAB) regional anesthesia if significant change of oxygenation occurs intraoperatively and postoperatively from the preoperative baseline level.

Technical Approach:

ASA I patients agreeing to SAB anesthesia will receive Diazepam 2 mg/kg by mouth one hour prior to induction of anesthesia. A single injection of hyperbaric tetracaine will be given using the midline or paramedian approach at level L3-L4. No further sedative medication will be given intraoperatively or postoperatively. Supplemental oxygen therapy will not be employed during the perioperative period. The ear oximeter, a noninvasive device for determining arterial oxygen saturation, will be used to determine oxygenation. One measurement will be taken the evening prior to surgery to serve as the baseline level. Two measurements intraoperatively and two measurements postoperatively in the recovery room will also be taken.

Any patient requiring additional intraoperative or postoperative sedation or requiring supplemental oxygen therapy during the perio-operative will be rejected from the sample. A sample mean will be determined for each measurement, and dependent on the number of the sample a student's t-test or a z-test of significance will be made. A table of percent change from baseline levels will also be included.

Progress:

A sample of 9 ASA I patients for surgical procedures requiring subarachnoid block anesthesia to the level of T8 or less were used. Each sample member had no history of lung disease or smoking. The pre-operative medication given was valium 0.2 mg/1 kg p.o. given about one hour prior to surgery. The initial readings of oxygen saturation were taken the evening prior to surgery, after the ear oximeter was calibrated per manufacturer's instructions, and recorded. Intra-operative and post-operative measurements were taken at 30 minute and 50 minute intervals from the time the SAB was placed and from arrival in the recovery room.

The subarachnoid block was administered in the lateral position after the lumbar area was appropriately prepared. The amount of pontocaine used to provide adequate anesthesia was determined by the patient's height. The dose range of 10-14 mg was used along with an equal amount of D₁₀W to provide adequate volume.

Percent O₂ Saturation

Pre-Operative		Intra-Operative		Recovery Rm	
Patients		30 min.	50 min		
1	97	91	Additional meds given no further readings		
2	95	93	"		
3	95	88	95	97	97
4	93	88	77	93	93
5	95	90	90	87	87
6	95	93	95	91	95
7	94	97	97	95	95
8	95	82	97	95	95
9	95	95	95	95	95

This study was undertaken to determine whether there was any significant change in the levels of oxygen saturation in patients undergoing SAB anesthesia. The results using the single tailed student's t-test showed no change, with one exception. The exception was noted in the first 30 minute sample where three patients, 3,4, and 8 had extreme shivering occur. The decrease in level of oxygenation was felt to be due to the shivering. The patients exhibited the resultant decrease in oxygen saturation due to increased oxygen consumption. These results then concur with the findings of previous studies.

Conclusion: The study indicates that there is no need for supplemental oxygen in most patients undergoing SAB anesthesia. The authors believe that there is sufficient evidence showing no change in oxygen saturation, that further study would not seem to be indicated.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/51 Status: Completed
 Title:
 Preoperative Anxiety and Continuity of Anesthesia Care

Start Date: Est Comp Date:
 Principal Investigator: Facility:

CPT R.C. Dahlander, ANC

Dept/Sec: Dept Nursing Assoc Investigators
 Key Words:

Anxiety

Accumulative MEDCASE Est Periodic
 Cost OMA Cost: Review Results
 Study Objective:

To determine whether patients counseled for general anesthesia by the anesthetist who will provide their anesthesia care have different levels of anxiety than patients similarly counseled by an anesthetist other than the one who will provide their anesthesia care.

Technical Approach:

A convenience sample of patients scheduled for surgery under general anesthesia will be selected. All patients will be ASA category I and scheduled for either abdominal or laparoscopic tubal ligation or inguinal hernia repair. All subjects will be between 18 and 50 years of age and be conversant in the English language. Patients with previous surgery, psychiatric histories, or who are drug abusers will be excluded. Between 20 and 40 subjects will be studied. Assignment of the experimental treatment will be at random. One group will receive a preoperative interview and counseling by the anesthetist who will care for them in the operating room the following day. The other group will receive a similar interview and counseling, but will be told that another person other than the interviewer will provide the anesthesia care the following day. These two treatments are usual procedure and are not unusual in any way. While patients are often seen by the person who will actually perform their anesthesia, it is also common practice for another anesthetist to see the patient due to scheduling or other manpower reasons. Voluntary consent will be obtained from each patients, if required by the Human Subjects Committee and the IPAT Anxiety Scale will be administered to each

subject between one and three hours after the preoperative interview. A raw score will be obtained for each subject. The mean of each group's raw scores will be obtained and subjected to statistical analysis. Subject participation will involve only the taking of a forty item paper and pencil test between one to three hours after the usual preoperative interview. Anesthesia care subsequent to the preoperative interview will not be manipulated or affected by the subjects participation or failure to participate.

PROGRESS:

A convenience sample of patients scheduled for surgery under general anesthesia was selected. All patients were ASA category I or II and scheduled for elective surgery. All subjects were between 18 and 49 years of age and were conversant in the English language. Patients with psychiatric histories, drug abusers, or patients on psychotropic drug therapy were excluded. Twenty-three patients were included. Those included in the study were asked to fill out and return the test instrument. Assignment of the patients to Group I or Group II was based on the last digit of their hospital numbers. Those patients having even hospital number last digits were placed in Group I and those with odd numbers Group II. All interviews were done by the primary investigator and were of similar content for both groups with the exception of the information regarding who would be caring for the patient the following day. Group I patients were told they would be cared for by the interviewer. Group II patients were told which named anesthetist other than the interviewer could be caring for them the next day.

The Spielberger Self-Evaluation questionnaire was given to each subject at the conclusion of the preoperative interview. Each subject was asked to fill out the questionnaire the evening before surgery and give it to a nursing unit staff member for placement in the patient's chart. The reliability and validity of the STAI is well established. It is a forty-item paper and pencil test yielding two subscores, the STAI-1 for state anxiety, the STAI-2 for trait anxiety. It is rapidly administered and scored. Two subscores were recorded for each subject. The means of each group's subscores were obtained and subjected to statistical analysis. The means for each group's subscores were obtained and subjected to the Student's t-ratio test, using the two sample case. An alpha of 0.01 was used. The mean scores for Group II were 38.3 for the STAI-1 and 39.3 for the STAI-2. The null hypothesis of no difference was not rejected. The trait anxiety subscores were similarly subjected to statistical testing. The null hypothesis was similarly accepted.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/52 Status: Completed

Title:

The Lawn Chair and Flat Positions and Their Relationship to Post-operative Back Pain

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT D.C. Simonson, ANC

Dept/Sect: Dept Nursing

Assoc Investigators

Key Words:

Back pain

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine if the position of the operating room table with respect to length of surgery has any relationship on post-operative back pain.

Technical Approach:

The sample population will be at least forty adults both military and civilian patients who do not have back pain at the time of surgery and who are not having back surgery. The patients will be placed in two groups: Group A will be patients placed in the lawn chair position and Group B will be patients placed on a flat operating room table. The lawn chair position will be a fifteen degree flexion of the thigh-back joint and a fifteen degree flexion of the knee-thigh joint in the reverse direction. A cardboard cutout will be utilized to make sure the table is set the same on each case. Patients will be assigned to groups according to the last digit of the hospital number. Group A will be even numbers and Group B will be odd numbers. Each patient will be required to sign a consent form to be eligible. On the night before surgery each patient will be asked "Do you have any pain at present in your arms, legs, back, or head" Those saying yes to having back pain will be eliminated from the project. On the day of surgery I will record the length of time the patient is on the operating room table, age, weight, height, ASA status, and type of surgery, and of course the position of the operating room table. Then on the day after surgery the ward nurse or myself will ask the patient the same question as asked preoperatively. The ward nurse will have no knowledge of the position of the operating room table. The responses will be

recorded. Data analysis will be done statistically using a Chi square table. The chart will be divided into surgery less than ninety minutes and surgery greater than ninety minutes. Also the responses about having or not having back pain will be recorded in the Chi square table.

Progress:

Patients were placed in two groups. Group A were those patients placed in the lawn chair position; Group B those in the flat position. Patients with an even last hospital number were placed in Group A and those with an odd number were in Group B.

In order to assure conformity in the contour position, a cardboard cutout with an angle of 15 degrees was used to determine the necessary flexion of the table.

The night before surgery each patient was asked: "Do you have any pain at present in your arms, legs, back, or head" Those who said "yes" to having back pain were eliminated from the study. On the day of surgery, the length of time the patient was actually on the table was recorded. The patient's age, weight, height, ASA status, and type of surgery performed were recorded. The day after surgery the ward nurse (who had no knowledge of what the patient's surgical position was) asked the question, "Have you been having any pain in your arms, leg, back, and head since surgery" The responses were recorded.

A result of the Chi-square test showing a p value of less than 0.01 was considered significant. The Chi-square table was constructed with a time variable in order to eliminate variability due to length of time on the table.

Sixty patients were included in the study. The length of time on the table ranged from 28 minutes to 5 hours. Patients' weight was normally distributed. The age of the patients ranged from 18 years to 72 years old. The surgical procedures performed included orthopedic, abdominal, gynecologic, and vascular surgery. The physical status category (ASA) ranged from ASA I to ASA III.

There were 21 patients in the less than 90-minute category, and 39 patients in the greater than 90-minute category. Chi-square analysis of the data for independence of variables demonstrated that there was no significant difference ($p < 0.01$) between the treatment and control group. The overall incidence of back pain was thirteen percent, which is somewhat smaller than that reported in earlier studies.

The data collected here does not support the hypothesis that the lawn chair position reduces the incidence of back pain. It appears that although the lawn chair position has some intuitive appeal, the solution to the problem of post-operative back pain may lie in other maneuvers or devices.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/50 Status: Ongoing

Title:
Hemolysis During Blood Administration

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL E. Sullivan, ANC

Dept/Sec: Dept Nursing Assoc Investigators

Key Words:

Hemolysis

Accumulative MEDCASE Est Periodic

Cost OMA Cost: Review Results

Study Objective:

To determine whether patients are receiving effective hemotherapy during blood administration. Determining if there is significant hemolysis may account for a patient's decreased response to blood therapy in the absence of detectable antibodies or stress related factors. Assumptions have been made regarding the size of the red blood cell and the diameter of the bore of different gauge needles for safe passage of red blood cells. Hemolysis has not been measured to assure the assumptions are valid using the current, improved equipment, recommended time(s) necessary for safe infusion, or with the different types of blood components in use today.

Technical Approach:

The research approach for this study will be experimental, for the in vitro portion of the study. The needles will be selected randomly from the container in which they arrive. The independent variables - type and gauge of the needle, use of filters, rate of infusion and type of blood products - will be actively manipulated to determine their effect on hemolysis, the dependent variable. The gauge of the needle and type of blood products will be studied in vivo only, because of their potential adverse effect on humans.

Twenty-thirty patients with leukemia will be selected for the study of platelet therapy, to minimize the bias of the disease process. The temperature of the infused platelets will be recorded as will the patient's history. Sixty patients from the MICU, SICU and Trauma Unit requiring whole blood transfusions will be studied as they appear and randomly compared, if possible, to similar patients who did not require transfusion. Sixty patients from the MICU, SICU and Trauma Unit requiring packaged red blood cells will also be

studied.

The Spielberger State and Trait Anxiety Tests will be used to measure the patients trait (normal) anxiety and the patients state anxiety that was experienced during and following blood administration. Permission was granted for the use of the STAI Form X-1 and X-2 by Dr Charles Spielberger.

Progress:

This protocol was approved late in FY81. Patient entry has just started.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 74/01 Status: Terminated

Title:

Umbilical Cord Lactate, Pyruvate, Betahydroxy Butyrate, pCO₂, pO₂, and pH value in Normal and Abnormal Pregnancies

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC W. Daniell, MC

Dept/Sec: Obstetrics-Gynecology

Assoc Investigators

Key Words:

Umbilical cord blood

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To study the effect of labor on normal pregnancies and pregnancies complicated by placental insufficiency.

Technical Approach:

Maternal amniotic fluid, venous, umbilical arterial and umbilical venous blood samples will be studied for the above levels. The results will be correlated with neonatal outcome and morbidity.

Progress:

The principal investigator has resigned. No patients were entered in this study.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 77/02 Status: Ongoing

Title:

Ultrastructural Investigation of Prostaglandins and Their Precursors
in the Human Fetal Chorioamnionic Membrane

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

B.E.F. Reimann, PhD, DAC

Dept/Sec: Obstetrics-Gynecology

Assoc Investigators

Key Words:

Prostaglandins; Chorioamnion

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$0 (140)

Review Results

Study Objective:

To determine if prostaglandins and their precursors can be localized
in fetal membrane and to detect any change with these in association
with labor.

Technical Approach:

Using indirect antibody labeling technique, prostaglandins were
tagged at a cellular level. The section was then imbedded and
ultrathin sections made.

Progress:

Technical support for research electromicroscopy was unavailable in
FY81. The project will be continued if manpower allows.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 77/04 Status: Completed

Title:
Inhibition of Premature Labor with Terbutaline

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC W.C. Daniell, MC

Dept/Sec: Obstetrics-Gynecology Assoc Investigators
Key Words:

Premature labor; Terbutaline

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To study inhibitory effects of terbutaline on premature labor.

Technical Approach:

Patients with no contraindicating condition, such as ruptured BOW, intrauterine sepsis, or abruptio placenta will be treated for premature labor with either Terbutaline or a placebo. After admission to the Labor and Delivery Suite, the following procedures will be initiated:

Terbutaline should be begun 0.25 mg subcutaneously every 3 hours. This dose may be increased to 1.0 mg subcutaneously every 3 hours as long as severe maternal tachycardia, hypotension or fetal distress do not result. When contractions are stopped, the dose and frequency should be reduced until patients are on 0.25 mg of terbutaline every 4 hours. Once they have been stable for 12 hours, they may be begun on oral terbutaline, 2.5 mg every 4 to 5 hours to maintain control. At this point, the patient may be transferred from Labor and Delivery to Ward 4P. Patients still having some uterine activity on this dose of oral terbutaline may be increased to 5.0 mg of terbutaline every 4 to 5 hours if tolerated. The oral terbutaline should be continued until 35 weeks estimated gestational age is reached, at which time it should be discontinued.

Progress:

No patients were entered in this study under the revised protocol. The principal investigator has resigned. Presentations and publications resulting from the data of patients treated intravenously appear in this FY, and previous FY tables. In the doses used, no difference in pregnancy outcome between treated and control groups was apparent.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 77/06 Status: Ongoing

Title:

Study to Determine the Ability of Amniotic Fluid to Inhibit Growth of E. Coli

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL David Boyce, MC

Dept/Sec: Obstetrics-Gynecology

Assoc Investigators

Key Words:

Amniotic fluid; Bacterial growth inhibition

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$482 (5442)

Review Results

Study Objective:

To devise an improved laboratory method for determining the inhibitory property of amniotic fluid.

Technical Approach:

The growth and/or inhibition of a laboratory strain of E. Coli in amniotic fluid as well as certain controlled media is to be monitored by a technique using C14 tagged glucose in the various culture media and monitored by the amount of 14 CO2 eluted as measured in a liquid scintillation counter. Maternal and cord blood serum zinc levels will be determined as well as the zinc and phosphate ratios of the amniotic fluid. An attempt will be made to correlate the inhibitory or noninhibitory effect of amniotic fluid on the E. coli as well as the zinc and zinc/phosphate ratios of this inhibitor effect to neonatal sepsis.

Progress:

Attempts to isolate and identify an inhibitory peptide have been unsuccessful. Work is continuing seeking correlation of bacterial inhibition demonstrated by this technique and patient outcome.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 77/19 Status: Completed

Title:

The Effect of Prostaglandin Synthesis Inhibitors on Uterine Blood Flow

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC W.C. Daniell, MC

Dept/Sec: Obstetrics - Gynecology

Assoc Investigators

Key Words:

Prostaglandins; uterine blood flow

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$2408 (5/08)

Review Results

Study Objective:

Determine effects of prostaglandin synthetase inhibitors on uterine blood flow in pregnant animals.

Technical Approach:

Application of three different categories of agents will be considered. The response of the uterine blood flow to specific arachidonic acids, prostaglandin synthesis intermediates, and prostaglandins. This is important because of the necessity to learn in what way the uterine blood flow is influenced by each class of compounds. The response of the uterine blood flow to substances with a known ability to block prostaglandin synthesis (e.g. acetylsalicylic acid or indomethacin). The response of the uterine blood flow to substances of unknown ability to block prostaglandin synthesis (e.g. phenylbutazone) or to substances which have shown, in varying studies, different reactions and consequently have yielded contradicting interpretations. Here particularly the cannabinoids must be included. Drugs to be tested in the study include: (1) estradiol (known to increase the uterine blood flow) (2) indomethacin (known to reduce the uterine blood flow) (3) acetylsalicylic acid (4) phenylbutazone (5) cannabinal (CBN) (6) cannabidiolic acid (CBD Acid) (7) (-)-trans- Δ^8 tetrahydrocannabinol (delta-8-THC) (8) cannabidiol (CBC) (10) (-)-trans- Δ^9 tetrahydrocannabinol (delta-9-THC) (11) cannabicyclol (CBCy) (12) olivetol (13) various prostaglandins (PGA, PGB, PGE, PGF family members). Both nonpregnant and pregnant sheep will have electric blood flow monitors implanted around the two uterine arteries. At the same time, catheters will be placed in both the

femoral artery and vein with their tips located in the common iliac artery or vein respectively. This surgical procedure is a routine operation of our team (e.g. see Killam et al 1973). After recovery of the animals from surgery, the ewes will be given estradiol to increase the uterine blood flow. Doses of indomethacin and acetylsalicylic acid are designed to give an indication of the general reaction norm of each animal. Doses of cannabinoids as indicated above, individually or in combination with other drugs, will be infused into one of the uterine arteries through the first branch of the uterine artery in the broad ligament. The measured parameters as a response to the medication are changes of pressure and flow rate, as recorded through the implanted instruments. The uterine vascular conductance will be calculated from the pressure-flow ratio:

$$\text{Conductance} = \frac{\text{Flow}}{\text{Arterial-venous pressure}}$$

Progress: The principal investigator has resigned but work done prior to his departure is summarized as follows:

New Zealand white rabbits, at 27 or 28 days gestational age, were studied. We anesthetized the animals with intravenous ketamine, 10 mg/kg, and supplemental doses as required. Nineteen gauge catheters were passed into the left ventricle via the right carotid artery and into the distal left femoral artery via arteriotomy. Catheter location in the ventricle was verified by pressure tracing. The location was documented at necropsy in the first several animals studied. We infused 150 μ l of a room temperature, mechanically mixed 25 ml stock suspension of 10 percent dextran and 0.05 percent Tween 80 containing ^{141}Ce labeled microspheres with an average diameter of $15 \pm 3\mu\text{m}$ and total radioactivity of 1 mCi. Blood was withdrawn at a constant rate of 1.23 ml/min from the femoral artery. Fifteen seconds later the microspheres were infused into the ventricle over a 30-40 second time interval. Withdrawal was continued for two minutes with the same pump at the same setting in every experiment. Right and left renal perfusion was measured at time zero and again at one hour in every animal as evidence of adequacy of mixing. Immediately following the initial microsphere infusion and withdrawal a control solution of five percent ethanol in normal saline or control solution test drug was infused into the left ventricle in a volume of 5 ml/kg and a rate of 1 ml/min. The drug concentration was adjusted to be a total dose of 1 mg (group 1) or 2 mg (group 2)/kg of $\Delta^9\text{THC}$. At one hour 150 μ l of ^{85}Sr microspheres were injected and samples were obtained as at time zero. Except for the isotope the strontium and cerium were identical. Blood pressure and heart rate were continuously recorded from a right femoral artery catheter placed as above in three animals from each of the $\Delta^9\text{THC}$ groups. The animals were killed with intravenous T61 solution immediately after the second isotope study. The tissue was counted whole in a dual channel counter equipped with a 3" crystal. Right and left renal cortex from superior to inferior poles and every placenta and adjoined portion of

uterus were included. Approximately 1 g of tissue was obtained from each kidney. The pooled placenta samples ranged from 2 to 3 g and the pooled uterine samples from 1/2 to 2 g. Tissue was weighed to the nearest mg. Perfusion was calculated using the formula (cpm organ \times 1.23 ml/min) (cpm blood \times g of organ). Except as noted in the text, statistical comparison was by Student's two-tailed paired t-test.

Baseline (T0) and one hour (T1) perfusion rates expressed in ml min⁻¹ gm⁻¹ (Mean \pm SD)

	Renal		Uterine		Placental	
	T0	T1	T0	T1	T0	T1
Δ^9 THC, 1 mg/kg ⁻¹ (n = 6)	4.53 \pm 2.03	2.99 \pm 0.88	0.16 \pm 0.03	0.11 \pm 0.05*	0.46 \pm 0.12	0.17 \pm 0.12***
Δ^9 THC, 2 mg/kg ⁻¹ (n = 8)	4.95 \pm 1.66	3.00 \pm 1.11***	0.22 \pm 0.19	0.19 \pm 0.14	0.45 \pm 0.27	0.17 \pm 0.14**

*P < 0.025 **P < 0.001 ***P < 0.001

Results and discussion: Since right kidney perfusion expressed as percent of left kidney perfusion was 99.5 \pm 10.9 percent in the animals reported, total renal perfusion was averaged and used for statistical analysis. Perfusion data from treated animals are summarized in the table. The median number of fetuses per doe was 7. Group 2 included a rabbit with two fetuses. The other animals shown in the table each contained five or more fetuses. With small litters, uterine perfusion rates were found to be inversely proportional to the number of fetuses. The larger means and standard deviation of uterine perfusion in group 2 reflects the higher perfusion rate in the single doe with less than five fetuses. Each animal in group 1 had decreased uterine perfusion, each animal in group 2 had decreased renal perfusion, and all 14 animals in both group Δ^9 THC groups had decreased placental perfusion (see figure, P < 0.01 by the sign test or the signed rank test, P < 0.001 by a paired t-test combining data of both groups (t = 5.12, (df 13))). The control group of seven animals did not significantly change renal, uterine or placental perfusion from baseline to one hour.

In group 1 arterial blood pH dropped from 7.28 \pm 0.05 to 7.23 \pm 0.10 (P < 0.05) and PaCO₂ increased from 35.8 \pm 5.2 to 45.0 \pm 4.5 (P < 0.005). There was no significant change in PO₂. Comparable changes plus a decrease of PaO₂ from 57.7 \pm 5.4 torr to 49.7 \pm 2.1 torr (P < 0.05) occurred in group 2. Average mean arterial blood pressure did not change in the control group or group 1, but decreased from 59 torr to 35 torr by 1/2 hour with a return to 45 torr by one hour (P < 0.01) in group 2. Mean heart rate decreased significantly (P < 0.001) and remained stable thereafter to one hour in both groups; from 220 to 133, and 227 to 153 beats/min in group 1 and 2 respectively. Mean serum concentrations of Δ^9 THC measured by radioimmunoassay in group 1 were 515 \pm 182 and 515 \pm 150 ng/ml at 1/2 hour and one hour respectively.

Consistent decreases in uterine perfusion, but not renal perfusion at the lower dose of Δ^9 THC suggest that the uterine response resulted from the drug rather than being secondary to a more generalized metabolic process. The general effects we monitored support this hypothesis. Similar blood gas changes were noted in an

indomethacin (0.5 mg/kg) group without perfusion decreases, and the 1 mg/kg Δ^9 THC group, with decreased uterine perfusion. Statistically significant hypotension did not occur in either group. Relative bradycardia occurred in both groups. A differential response is also suggested by a more significant decrease of placental than of uterine perfusion, at 1 mg/kg Δ^9 THC, and by continued inhibition of placental perfusion, but not uterine perfusion, at 2 mg/kg of Δ^9 THC. Hypoxemia has been reported to decrease renal and placental, but not uterine, perfusion in the rabbit, and not until PaO_2 decreases to 35 torr. In this study after 2 mg/kg of Δ^9 THC less severe hypoxemia developed in the presence of acidosis and hypercapnia, but the same pattern of perfusion effects occurred. In the 2 mg/kg Δ^9 THC group hypotension was statistically significant throughout the post-infusion one-hour study period. However, it was not significant compared to published data regarding decreases in blood pressure necessary to effect combined uteroplacental blood flow in pregnant rabbits. Relative bradycardia was no more pronounced in the 2 mg/kg than the 1 mg/kg Δ^9 THC group. In addition to hypoxemia and hypotension, another potential confounding variable at higher doses may be an indirect or direct uterotrophic effect of Δ^9 THC.

Our observations in the rabbit are consistent with those in the primate in that factors which regulate uterine and placental blood flow appear to act independently. At 2 mg/kg of Δ^9 THC we noted effects similar to the relative myometrial hyperemia and placental ischemia reported by this group, who used oxytocin and prostaglandin E_2 in pregnant primates. In general, our results from discrete time measurements suggest effects on rabbit uterine and placental perfusion which mimic prostaglandin $\text{F}_{2\alpha}$ at 1 mg/kg of Δ^9 THC and prostaglandin E at 2 mg/kg of Δ^9 THC. Further experiments will be required to study the dose relationship and mechanism of inhibition of uterine and placental perfusion by Δ^9 THC. Our data, adjusted for dose, correlates with reported serum concentrations following intravenous Δ^9 THC in rabbits. The doses of Δ^9 THC we infused produced blood levels near those reported after a single marijuana cigarette in humans. Higher acute levels of active compounds are possible in marijuana users. Cumulative effects may also differ from short term effects, as may effects in habitual as opposed to occasional users. Species differences, or lack of differences, in perfusion responses are not predictable. Our data do not prove a primary effect of Δ^9 THC on uterine or placental perfusion in the pregnant rabbit, but we have shown decreases in uterine perfusion following apparent physiologic dose of Δ^9 THC. These effects whether primary or secondary, could have important consequences if similar changes occur in pregnant human marijuana users.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 11/25 Status: Ongoing

Title:

A Comparison of Phospholipid Levels and Choline Phosphotransferase (CPT) Activity in Amniotic Fluid and Newborn Tracheal Fluid

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC W.C. Daniell, MC

Dept/Sec: Obstetrics-Gynecology

Assoc Investigators

Key Words:

Phosphatidylglycerol; Amniotic fluid

COL L.L. Penney, MC

David O. Rauls, PhD, DAC

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$11/2 (5911)

Review Results

Study Objective:

To determine if the level of phosphatidyl glycerol (PG) and phosphatidyl inositol (PI) or the activity of choline phosphotransferase could serve as an accurate index of lung maturity.

Technical Approach:

Amniotic fluid, and neonatal gastric and pharyngeal fluids which are normally discarded, will be analyzed for phosphatidyl glycerol, phosphatidyl inositol, choline phosphotransferase, and magnesium. The levels measured will be correlated with the incidence and severity of neonatal respiratory stress and hyaline membrane disease.

Progress:

A rapid analysis for PG in amniotic fluid has been developed and is being evaluated for clinical applicability. The associate investigators have assumed the protocol as the principal investigator designated above has resigned.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 78/25 Status: Completed
 Title:
 Inhibition of the Vascular Effect of 1/β estradiol with
 Actinomycin D
 Start Date: Est Comp Date:
 Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Obstetrics-Gynecology Assoc Investigators
 Key Words:

Estradiol; Uterine blood flow; Actinomycin D

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost: \$1405 (5813)	Review Results
Study Objective:		

To determine if the vascular effect of 1/β estradiol employs the same pathways as the growth promoting effect on the sex organs of rabbits.

Technical Approach:

Actinomycin D will be given to rabbits in sufficient dosage to block the growth promoting effect of estradiol 1/-beta, which is a potent vasodilator of the uterus as well as a potent growth promoter. If the vascular effect of estradiol-1/-beta is not affected nearly as much as the growth promoting effect, this would suggest that the vascular effect does not rely on transcription. Study rabbits will be divided into random groups, all will initially have their ovaries removed. A femoral artery and a carotid artery will be catheterized. Baseline uterine blood flow will be determined by infusing 10-15 μCi ¹⁴Ce microspheres in the carotid catheter and sampling from the femoral artery. Ten μg/kg of 1/β estradiol with labeled uridine will be given and the control animals subdivided for study at hourly (or less if needed) intervals to determine onset of increased blood flow. An infusion of 30-40 μCi ⁸⁵Sr at these intervals will be used to calculate blood flow. All animals will then be sacrificed and aliquots of uterine tissue for RNA quantitation and label incorporation will be analyzed. The microspheres per gram of uterine tissue and per organ will be determined. Subsequently repeat blood flow studies will be done at the time at which control animals increased their uterine blood flow. These animals will receive actinomycin 4 mg/kg, cycloheximide 20 mg/kg, or puromycin 200 mg/kg 30 minutes prior to hormone administration.

Progress:

The 1/ β -estradiol-induced increase of uterine blood flow (UBF) was studied in 7- to 8-month-old oophorectomized rabbits 5-39 days after operation. Baseline blood flows were determined with ^{141}Ce -labeled microspheres and 2-h flows with ^{85}Sr -labeled microspheres. Mean UBF in control groups ranged from 0.11-0.25 ml/min. g. Mean UBF 2 h after 1/ β -estradiol (10 $\mu\text{g/kg}$ BW) was 1.51 ml/min.g. Utilizing [^3H] uridine (100 $\mu\text{Ci/kg}$ 15 min before the 2-h flow study), ^3H incorporation into uterine RNA was 2-fold higher than background. Estradiol treatment produced a 4-fold increase in ^3H incorporation into uterine RNA. Estradiol-treated animals, pretreated with actinomycin D (4 mg/kg), increased UBF to 1.09 ml/min.g 2 h after estradiol but failed to increase uterine RNA synthesis. ^3H incorporation into uterine RNA in this group was suppressed to undetectable (background) levels. These findings indicate that a mechanism other than accelerated transcription, whether induced directly or by translocation of a cytosolic receptor, underlies the increased UBF after estradiol administration to oophorectomized rabbits.

This data suggests other research approaches which will be pursued under protocols 81/45, 81/47, and 81/48.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/04 Status: Completed

Title:

Prevention of Post-Cesarean Section Infections

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC W.C. Daniell, MC

Dept/Sec: Obstetrics-Gynecology

Assoc Investigators

Key Words:

Cesarean section; Prophylactic antibiotics

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine whether the routine administration of Cephalin will lower the incidence of post-cesarean section infectious morbidity. There is a 30-40 percent incidence of infectious morbidity if a woman is delivered by cesarean section following labor with ruptured amniotic membranes for longer than six hours. Prophylactic administration of antibiotics to patients undergoing vaginal hysterectomy has significantly reduced the rate of infectious morbidity. It is hoped that an antibiotic regimen can be discovered which will reduce the infectious morbidity associated with cesarean section. The cephalosporins have been used extensively for prophylaxis with vaginal hysterectomy. Cephalin was chosen because a single dose given prior to vaginal hysterectomy has been shown to be at least as efficacious as the standard 3-dose regimen with cephaloridine. Other studies involving antibiotics for post-cesarean section infections have not shown a consistent, significant lowering of morbidity. However, patients not in labor or in labor for long periods of time have been included in these studies. We have selected a very high risk population and will test a 1-dose regimen against a control population. Only those patients who have had ruptured BOW, labor, and intrauterine monitoring prior to delivery will be entered in the study group.

Technical Approach:

When a woman is entered into the study she will be placed into one of two drug regimen groups. A control who gets a single injection of a placebo intravenously at the time of cesarean section, another group who gets a single shot of Cephalin, 1 gram IV at the time of cesarean section. Upon discharge, both the mother's and infant's charts will be reviewed by a member of the perinatal staff and a listing of all the complications compiled from a data sheet included in the study and the chart itself. Patients with previous allergic reaction to penicillin will not be included in the study.

Group I: Placebo at the time of cesarean section.

Group II: Cephalin, 1 gram IV at the time of cesarean section. Additionally, in conjunction with Dr. Boyce's study on the influence of amniotic fluid on bacterial growth, small samples of amniotic fluid will be obtained through the monitoring catheter which is routinely emplaced upon admission to the Labor and Delivery suite. The inhibitory effect of these individual specimens with particular attention to zinc levels, will be related to the ultimate result in infectious morbidity. We hope to define groups of low and high risk, one group benefitting from prophylactic antibiotic therapy.

Progress:

Eighty-four patients were entered in this study. Of 32 patients with culture data 2/14 with no growth and 8/14 with growth became infected. No abscesses and only one case of endometritis occurred. Febrile morbidity was noted in 29/84 cases equally distributed between treatment and control groups. It is concluded that a single dose of 1 gm of cephalin IV is ineffective antibiotic prophylaxis when given immediately after cord clamping during Cesarean section.

Detail Summary Sheet

Date: 1 Oct 81	Prot No: 80/9	Status: Ongoing
Title: Effect of Terbutaline on Surface Active Phospholipids in Adult and Fetal Lung		
Start Date:	Est Comp Date:	
Principal Investigator: D.O. Rauls, PhD, DAC	Facility:	
Dept/Sec: Obstetrics-Gynecology	Assoc Investigators	
Key Words: Terbutaline; Surface active phospholipids		
Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost: \$0 (1040)	Review Results
Study Objective:		

To determine if administration of Terbutaline affects lung maturation profile in adult dog and fetal rabbit lungs.

Technical Approach:

Anesthetized adult beagle dogs will be studied in the first phase of the project. They will be given .5 mgm Terbutaline or placebo in 250 cc of saline over a two-hour period. Tracheal bronchial washings using saline will be done at zero, two, four, and six hours and the washings saved and analyzed for surface active phospholipid content to determine if acute infusion of Terbutaline has affected the phospholipid content in the lungs. In phase two, pregnant rabbits with immature fetuses will be given Terbutaline or a placebo subcutaneously over a 3-day period. The animals will then be sacrificed and the fetal and adult lungs will be studied for surface active phospholipids to determine if a change has occurred.

Progress:

The effect of the beta-2-adrenergic receptor agonist terbutaline on the phospholipid composition of anesthetized adult beagle dog tracheal wash was studied. Adult beagle dogs were anesthetized with sodium pentobarbital and administered either 0.9% saline or 0.5 mg of terbutaline in 250 ml of 0.9% saline over a two hour period. A pulmonary lavage was performed with 50 ml of 0.9% saline and the phospholipid composition of the lavagate was determined. Percent composition data revealed little effect of the drug on surfactant composition. Calculation of phosphatidylcholine/sphingomyeline (L/S) ratios revealed a significant ($p < 0.05$) decrease in the L/S ratio one hour after terbutaline administration. The results indicated that when studying the effects of drugs on pulmonary surfactant quality one must consider the effects on the entire spectrum of phospholipids present rather than on phosphatidylcholine alone. Six additional dogs will be studied in an attempt to substantiate the reported results.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/17 Status: Ongoing

Title:

Transvaginal Absorption of Estrogens in Patients Following Pelvic Irradiation

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ H. Greenberg, MC

Dept/Sec: Obstetrics-Gynecology

Assoc Investigators

Key Words:

Estradiol; Estrone

COL L.L. Penney, MC

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$1315 (2090

Review Results

Study Objective:

To quantitate serum levels of 1/ β -estradiol and estrone following vaginal application of the appropriate cream in patients who are post-irradiation of the vaginal epithelium.

Technical Approach:

Patient volunteers who have received pelvic irradiation for nonestrogen dependent neoplasms will be studied. All estrogen medications will be withdrawn for four weeks. Eight to ten patients will be divided into two groups randomly. One group will receive Premarin 1.25 mg and the other Estrace 2 mg intravaginally. Baseline serum estrone and estradiol concentrations will be obtained and repeated at 30 minutes and at one hour, two hours, four hours, eight hours, and 24 hours following the medication. One week later the groups will be reversed. Insofar as possible, patients will be matched regarding age, diagnosis and amount of irradiation received.

Progress:

Rapid transvaginal absorption of estradiol through irradiated mucosa has been documented. The samples are currently being analyzed for estrone.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/25 Status: Ongoing

Title:

Placental Levels of 5 α -dihydroprogesterone in Normal Pregnancy and Those Complicated by Pre-eclampsia

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

David O. Rauls, PhD, DAC

Dept/Sec: Obstetrics-Gynecology

Assoc Investigators

Key Words:

Dihydroprogesterone; Pre-eclampsia

Accumulative MEDCASE

Est

Periodic

Cost \$6,603

OMA Cost:\$45(345)

Review Results

Study Objective:

To determine if placentas of pregnancies complicated by pre-eclampsia have a different concentration of 5 α -dihydroprogesterone than those of uncomplicated pregnancies.

Technical Approach:

Placentas from normal and pregnancies complicated by pre-eclampsia will be studied for their content of 5 α -dihydroprogesterone. After consent has been obtained from patients who are admitted in labor, the placentas obtained at birth will be drained of blood and the membranes excised. They will then be weighed and, using the mass-spectrometer, presence and concentrations of 5 α -dihydroprogesterone will be determined. Concentration of 5 α -dihydroprogesterone in pregnancies complicated by pre-eclampsia will be compared to that of normal pregnancies. Twenty patients in each group will be studied initially and the mean levels of 5 α -dihydroprogesterone will be compared by Student's t-test.

Progress:

The GC-MS was inoperable much of FY80 due to construction and electrical-mechanical modifications with the Department work will be resumed when the equipment is again functional. A new principal investigator has assumed this protocol.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/03 Status: Ongoing

Title:

Serial Measurement of Serum, Zinc, Magnesium, Copper, Lead, Lithium and Arsenic During Pregnancy.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC R.W. Cotterill, MC

Dept/Sec: Obstetrics-Gynecology

Assoc Investigators

Key Words:

Trace elements

Accumulative MEDCASE
Cost

Est
OMA Cost: \$1081(1801

Periodic
Review Results

Study Objective:

To determine the serum levels of certain trace elements during each trimester of pregnancy in patients from the El Paso area. Specific goals will include: (1) Comparison of the serum levels of trace elements in two populations of patients, first the U.S. Army dependent population; second the native population of Thomason General Hospital. (2) To establish normal mean levels of zinc, magnesium, copper, lead, lithium, and arsenic at various stages of pregnancy. (3) To suggest future studies correlating the findings of serum levels of trace elements with pregnancy outcome.

Technical Approach:

The plan will be to determine the serum levels of copper, zinc, magnesium, lithium, lead and arsenic during the first trimester, again at 20 weeks gestation, and at term. In addition, fetal levels as determined by cord blood at delivery will be obtained. These values will be compared with nonpregnant controls.

Two separate patient populations will be compared, those of William Beaumont Army Medical Center and those of R.E. Thomason General Hospital. The two populations may reflect different levels of environmental exposure to these trace elements, as well as a possible difference in dietary intake.

a. The study would include approximately 50 pregnant patients from the OB Service, WBAMC, and a similar number of patients from the El Paso County population of RETGH.

b. Controls would be nonpregnant females of similar ages.

c. The investigation would include sampling of 10 cc venous blood at the following intervals during pregnancy: 1st trimester, mid-trimester, time of labor and delivery, and cord blood at delivery.

d. Sampling of controls at one time.

e. A questionnaire stating the historical data pertinent to each patient will be distributed. This will request the information regarding birth place, location of residence, and employment.

f. Additional control - the studied pregnant patients will be tested at six to 12 weeks postpartum.

Progress:

Serial sampling continues. Entries will be discontinued to allow completion of sampling in the second quarter of FY82 and data analysis in the third quarter

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/44 Status: Ongoing
Title:
Effect of Intravenous Terbutaline on Phospholipid Content of Adult Dog Lungs

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC R.W. Cotterill, MC

Dept/Sec: Obstetrics-Gynecology Assoc Investigators
Key Words:

Terbutaline; Surface active phospholipids

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

This study is designed to determine if intravenously administered terbutaline will cause a change in the concentration of phospholipids known to be important in the surfactant system of adult lungs.

Technical Approach:

Two groups of 8 mixed sex adult beagle dogs each will be used in the study. One group will receive 250 ml of 0.9 percent NaCl intravenously over a 30-minute period; these will serve as controls. One-half of these animals will be sacrificed at one hour, and the other half at four hours. The other group will receive 250 ml of 0.9 percent NaCl containing 0.5 mg of terbutaline intravenously over a 30-minute period and will be similarly sacrificed. Portions of lung and alveolar washings from each animal will be freshly obtained and studied for content of total phospholipid, lecithin, sphingomyelin, phosphatidyl inositol and phosphotidyl glycerol. We will then compare the groups to determine any changes in the phospholipid content over the period of time that we investigated.

Progress:

This protocol cannot be activated until sufficient animal holding space is available.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/61 Status: Ongoing

Title:

Maternal and Fetal Effects of Verapamil, A Calcium Blocking Agent

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

Daniel L. Vaughn, M.D.

Dept/Sec:

Assoc Investigators

Key Words:

Verapamil

Accumulative MEDCASE
Cost

Est
OMA Cost: \$1230(1230)

Periodic
Review Results

Study Objective:

This project is designed as a preliminary study to evaluate the effect of Verapamil on cardiovascular functions in pregnant ewes and their fetuses. Based on these findings, further studies will be done on the use of Verapamil as a tocolytic agent in the prevention of premature labor.

Technical Approach:

Ten near term pregnant ewes will be used. Spinal anesthesia will be administered using 8 mg xylocaine and light sedation obtained by giving 10 mg diazepam intramuscularly. Under separate local anesthesia, one carotid artery and jugular vein will be cannulated. The carotid catheter will serve to monitor maternal arterial pressure and heart rate and to collect arterial blood samples anaerobically. The jugular vein catheter will be used to monitor venous pressure and to administer Verapamil. The pregnant uterine horn will then be exposed through a midline incision and marsupialized to the abdominal wall to prevent evisceration. The fetus will then be delivered and marsupialized to the edges of the uterine incision to protect the umbilical circulation. The head will be covered with a saline-filled glove to prevent respirations. An indwelling catheter will be placed into an umbilical vein through an intercotyledonary branch and serve for anaerobic collection of umbilical vein blood samples and for monitoring the umbilical vein pressure.

The fetal femoral artery and vein will be cannulated; the femoral artery catheter will serve for the collection of blood samples and for monitoring fetal arterial pressure and heart rate. The venous catheter will serve for replacing blood collected for blood gases

with like volumes of maternal blood. Finally, an abdominal incision will be made in the fetus just above the cord attachment. Through this incision the umbilical vein will be exposed and a flow transducer attached. Local anesthesia will be used for the fetal surgery.

Following surgical preparation and stabilization of cardiovascular functions, a 30-minute control period, followed by a 2-hour experimental period of Verapamil administration, followed by a 30 minute recovery period will be conducted. Each animal will serve as its own control and the following parameters will be monitored:

- Maternal:
1. Arterial blood pressure
 2. Heart rate
 3. Venous blood pressure
 4. Arterial PO_2 , PCO_2 , PH, O_2 saturation, and base excess
 5. Umbilical vein PO_2 , PCO_2 , PH, O_2 saturation and base excess
 6. Umbilical vein flow

Verapamil will be administered intravenously at the rate of 0.1 mg/kg as a bolus dose, followed by 0.005 mg/kg/min in a continuous infusion. These doses are considered therapeutic in humans.

At the end of the experiment, the ewe and fetus will be sacrificed by the administration of a saturated solution of KCl intravenously.

It is felt that this experimental design will allow the detection of any significant derangement of cardiovascular or placental function resulting from Verapamil administration.

Progress:

Twelve pregnant sheep have been purchased. They will begin reaching the appropriate gestational age for this study in January 1982.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 76/24 Status: Ongoing

Title:

An Investigation of the Effects of Supplemental Oxygen on Chemically Induced Fat Embolization

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL D.A. Vichick, MC

Dept/Sec: Orthopedics

Assoc Investigators

Key Words:

Embolization; Oleic acid

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine whether or not supplemental oxygen prevents or lessens the potentially lethal effects of chemically induced fat embolization in dogs.

Technical Approach:

Clinical observations, as well as lung scans, are generally accepted as criteria for determination of the presence of fat embolism syndrome. In this study laboratory parameters and lung scans are obtained for five-day periods in beagles following injection of oleic acid. This data is collected from dogs supported on either room air or supplemental oxygen.

Progress:

Equipment for nuclear imaging in animals was acquired in FY81 and was fully operational by the fourth quarter. This study may now be conducted.

Detail Summary Sheet

Date: 1 Oct 31 Prot No: 79/03 Status: Ongoing

Title:

Compartmental Pressure Studies as a Determinant for the Need for
Fasciotomy

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL D.A. Vichick, MC

Dept/Sec: Orthopedics

Assoc Investigators

Key Words:

Fasciotomy

Accumulative MEDCASE

Est

Periodic

Cost \$5,430

OMA Cost:

Review Results

Study Objective:

Trauma (insult) to muscles will be followed by an injury reaction resulting in swelling (interstitial)(intercellular) of the involved muscle or muscles. If the traumatized muscles are contained within a nonyielding compartment, increased intracompartmental pressure can reach a level where it exceeds perfusion pressure (diastolic or venous pressure) although distal pulses may be present. As the pressure within the compartment approaches the systolic pressure of the patient there is no tissue perfusion and the distal pulses are absent. Studies in dogs have shown that the tissue injury increases as the duration of the ischemia increases. The impedance of capillary flow and venous drainage will set a stage for increased swelling followed by increased venous blockage until the intracompartmental pressures can exceed the arterial pressure in the small vessels of the involved muscles. The state of ischemia caused by the increase in intracompartmental pressure can lead to necrosis and death of the involved muscles.

Clinical experience has demonstrated the ability to prevent muscle necrosis as a result of increased compartmental/intracompartmental pressure by performing a fasciotomy thus converting the closed and nonyielding space to an expandable area. The clinical parameters of compartment syndrome are: (a) increased circumference of the extremity. (b) Increased pain of the involved area out of proportion to the injury and accentuated by voluntary motor effort. (c) Decreased motor power of the involved muscle group. (d) Decreased distal sensation. (e) Decreased quality of distal pulses.

The clinical criteria for a fasciotomy do not possess a high degree of sensitivity in indicating the necessity for fasciotomy. Thus errors of omission (delaying fasciotomy too long) and commission (performing fasciotomy when it is truly not needed) are still more frequent than desirable. It has been determined by Whitesides, et al., that as tissue pressure readings equal or exceed 30 millimeters of mercury, the patient must be carefully followed with periodic tissue pressure readings and monitoring of all signs and symptoms of a closed compartment syndrome. Further, as tissue pressures approach or equal the patient's diastolic pressure, a fasciotomy is definitely indicated. Tissue pressures of 40-45 mm of mercury should usually be the upper limit prior to fasciotomy when the diastolic pressure is in the range of 70mm of mercury. It was found that tissue recovery is essentially complete after four hours of ischemia, but only 50 percent complete after six hours of ischemia. The damage is extensive and irreversible after eight hours of ischemia. The contained neurotissues are even more sensitive to ischemia than muscle and thus the duration of ischemia is even more critical following prolonged increase of intracompartmental pressures.

A study will be conducted in which intracompartmental pressures of the anterior and posterior compartments of the legs, anterior and posterior compartments of the forearm, and dorsal interosseous compartments of the hand will be measured in various states of normal, stress and following disease or injury. The intracompartmental pressure values will be correlated with the clinical picture (pain, increased circumference, decreased motor activity and/or sensation, and quality of distal pulses). When possible and feasible, the uninjured extremity will be used as a control. During this study, fasciotomy will be performed using the accepted clinical indications without regard to the values as determined by the intracompartmental pressure studies alone.

Three categories of patients will be tested, each group consisting of 25 but not more than 50 patients. The categories will be as follows:

Group 1: Normal volunteers (or noninvolved extremities of Group 3 patients).

Group 2: Volunteers who will perform strenuous physical activity with the involved extremity while compartmental pressures are monitored: before, during and after activity.

Group 3: Volunteer patients who by way of disease or injury are suspected of having increased compartmental pressures of the lower leg, forearm, or dorsum of the hand.

A 22 or 24-gauge intracath will be inserted into the compartments to be studied or in question, both in the lower and upper extremity following a sterile preping of the area. The site selected for insertion will be determined by the investigator. The areas where muscle is felt to be compromised or to be normal will be studied primarily. Areas that closely surround fractures or known hematomas will be avoided if possible. The exact technique for recording intracompartmental pressures will be same as described by Matsen et al. During the study the compartment pressures will be obtained and correlated with the clinical picture, a determination will be made as to whether intracompartment pressures offer a significant advantage in determining the need for fasciotomy over known clinical parameters. The risk of the study to the volunteer participants is considered to be minimal and no greater than would occur with any intramuscular injection with a small bore needle.

Progress:

An abstract for the presentation of the data collected during the past three years has been submitted for presentation at the Annual Meeting of the Western Orthopaedic Association, Oct 1982. Inpatient records are currently being collected to review the data compiled during the past three years. Neither statistics nor a statistical analysis are available to report at this time.

Compartmental monitoring as a tool for aiding the diagnosis of compartment syndromes will continue to be ongoing. However, the formal study will end upon completion of the above mentioned paper. At that time, the accumulated data, results and analysis will be submitted to the Department of Clinical Investigation and the requested clinical investigation study will be completed.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/42 Status: Ongoing

Title:

The Incidence of Visual-Motor Perceptual Problems in Persons with Traumatic Hand Injuries

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ M.J. Baker, AMSC

Dept/Sec: Orthopedics

Assoc Investigators

Key Words:

Trauma, Hand

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine if persons with traumatic hand injuries have pre-existing visual motor perceptual problems which may have led to their trauma.

Technical Approach:

It is recognized by the Federal Government, school systems, and medical professionals that children may suffer from minimal brain dysfunction and/or developmental disabilities resulting in sensory-motor integration problems or inability to perform classroom and play activities in a manner appropriate for their age. In interviews of individuals with traumatic hand injuries it appears that these individuals may not know where their hands are in space and, therefore, suffer from a visual-motor perceptual problem, a form of sensory-motor integration.

The Slosson Drawing Coordination Test is reported to "screen out individuals suffering from serious forms of brain dysfunction or damage where eye-hand coordination is involved." "A reliability coefficient of .96 was obtained for a group of 200 individuals, aged 4 to 52 years." This test does not screen out individuals with emotional problems due to brain dysfunction nor does it identify individuals with eye-hand incoordination due to a specific visual-motor perceptual problem. The Kinesthesia Test of the Southern California Sensory Integration Test is intended to measure the capacity to perceive joint position and movement. Although this test is standardized for individuals from 4 to 8 years of age, it is felt to be an indicator of individuals unable to perceive their extremities in space, that is, visual-motor perceptual dysfunction.

a. The specific purpose of this study is to determine if individuals with traumatic hand injuries also have a pre-existing visual-motor perceptual problem as measured by the Slosson Drawing Coordination Test and the Kinesthesia Test of the Southern California Sensory Integration Tests.

b. The number of subjects for the study will be 20 persons with traumatic hand injuries. The age range of these individuals will be 18 to 30 years of age; they will be active duty military, males and females.

Progress:

Ninety-three patients have entered. Entry and subsequent data analysis will be completed by the third quarter FY82.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/6 Status: Completed

Title:

Evaluation of Antagonistic Knee Flexors and Extensors During Prone and Supine Resistive Exercises Using Electromyography

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ William R Smith, MC

Dept/Sec: Orthopedics

Assoc Investigators

Key Words:

Electromyography; Knee

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

The rehabilitation of post-operative patellectomies at this institution has in the past involved the use of straight leg-raising with isometric quadriceps exercises. One significant complication of this approach has been the disruption of the operative repair. These exercises are typically performed with the patient in the supine position. One obvious question which we asked was whether prone exercises would facilitate active joint motion while concomitantly reducing the strain on the surgical site and thus minimize the possibility of rupture of the repair. This type exercise is now being performed and the objective of this study is to ascertain the degree of muscular activity in the antagonistic muscle group (i.e. hamstrings versus quadriceps) with resistive exercise in a supine or prone position utilizing the technique of electromyography.

Technical Approach:

A study will be performed in which the quantity of electromyographic activity of the quadriceps and hamstring muscle groups will be monitored while normal volunteers undergo both prone and supine knee exercises with flexion and extension, respectively, against varying weight on their ankles. In addition, both fast and slow extension and flexion will be performed. A TECA Model 4 Electromyograph with a preamplifier secured to both the anterior and posterior thigh at the area of greatest muscle bulk (approx. mid-thigh) while the surface anode electrode will be placed approximately 1 1/2 inches distal to the cathode. Then, the two tracings will be displayed on the electromyograph simultaneously. The volunteers (10 in number)

will then be asked to perform knee flexion (free and against increasing weights at 10, 20, 30 lbs) and extension while in the prone and supine positions respectively. The volunteers will serve as their own control with the free movement. The grading system of EMG activity will be that used by Basmajian and Murphy. In addition the absolute activity in microvolts will be read from the oscilloscopic output of the TECA EMG and recorded. The data will then be assessed for level of significance using the student's paired t-test.

Progress:

Results of this work were presented at the SOMOS Meeting in San Antonio, Texas, in November 1980. There were ten patients entered into the study, and the patients served as their own controls. The results suggested that higher evoked motor potentials were obtained with rapid exercise modes and that the amount of activity noted in the quadriceps muscle group with prone flexion exercise was minimal. The application of this study to our orthopedic department has been invaluable in maintaining knee motion with prone exercises and minimizing pull of the quadriceps on our operative knee cases such as patellar realignments.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 70/111 Status: Completed

Title:

Molecular Etching

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

B.E.F. Reimann, DAC

Dept/Sec: Pathology

Assoc Investigators

Key Words:

Molecular etching

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$0 (1040)

Review Results

Study Objective:

To obtain general information on the ultrastructure of biological membranes (in particular the erythrocyte membrane) and other cellular organs in order to discern their structural changes under varying experimental (and disease related) conditions and, for this reason, to develop techniques by which the biological material can be investigated in the least altered state employing methods such as freeze drying and ionic etching in conjunction with electron microscopy.

Technical Approach:

The final goal is to subject lyophilized embedded biological material to a bombardment with accelerated ions or atoms and to reveal the obtained structures by electron microscopy. Presently the experiments are primarily concerned with osmotic pressures of erythrocytes employing freezing point depression osmometry an direct measurements with a Pfeffer's cell. A "critical point" drying chamber has been constructed.

Progress:

Publications and presentations from this protocol have been referenced or detailed in previous years. A new protocol will be submitted for any additional work.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 77/10 Status: Ongoing

Title:

Zinc Levels in Maternal Infant Pairs

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL L.L. Penney, MC

Dept/Sec:

Assoc Investigators

Key Words:

Zinc; Trace elements

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$800(4479

Review Results

Study Objective:

To determine the zinc level in maternal-infant pairs and to see if there is a correlation with the incidence of infection.

Technical Approach:

Zinc and phosphate concentrations in maternal and neonatal cord blood will be correlated with the incidence of neonatal sepsis in a blind retrospective study. The hypothesis of increasing zinc and phosphate levels in enhanced amniotic fluid bactericidal activity will be studied.

Progress:

Additional samples have been analyzed but data collection is extremely slow due to difficulties with retrieval of patients' charts.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 77/13 Status: Ongoing

Title:

Investigation of the Effects of Diphenylhydantoin on Intellectual Functioning of Children

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC P.F. LoPiccolo, MC

Dept/Sec: Pediatrics

Assoc Investigators

Key Words:

Diphenylhydantoin

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine if Dilantin has any effect on intellectual functioning.

Technical Approach:

To test children over the age of six years who have been placed on phenobarbital or dilantin because of a new seizure disorder. To test children who have been on long term anticonvulsants to see if there has been any change in intellectual function. This can only be accomplished if children had educational and psychological evaluations before the onset of their seizure disorder. Testing is being accomplished by Psychology using the WISC-R. The first part of the study has gone slowly because we have had very few cases of new spontaneous seizure disorders in children over the age of six years.

Progress:

Twenty patients have been entered. Larger numbers will be necessary to draw meaningful conclusions.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 78/14 Status: Completed

Title:

Maintenance of Patency of the Ductus Arteriosus in Congenital Cardiac Lesion

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC William Pearl, MC

Dept/Sec: Cardiology

Assoc Investigators

Key Words:

Prostaglandin E₁; Ductus arteriosus

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To maintain patency of the ductus arteriosus in infants with congenital heart disease, by infusing prostaglandin until diagnostic studies are completed and surgery can be arranged.

Technical Approach:

Prostaglandin E is the only nonsurgical treatment available for treatment of certain congenital heart defects such as maintaining patency of the ductus arteriosus until cardiac abnormalities in newborn infants can be surgically corrected. In infants in whom blood is flowing through the ductus from the aorta to the pulmonary artery, a catheter will be placed through the umbilical artery to the first part of the descending aorta, at or just above the ductus. Prostaglandin E₁ will be infused continually into this region at the rate of 0.1 micrograms per kilogram per minute. In infants in whom blood flow is passing through the ductus from the pulmonary artery to the aorta, a catheter will be placed in the pulmonary artery just beyond the ductus arteriosus, and the Prostaglandin E₁ will be infused at the rate of 0.1 micrograms per kilogram per minute. In the event that the major artery cannot be catheterized, the infusion will be given into a large vein, and the investigator will be asked to observe the infant closely for any systemic effects. The infusion will be continued until surgery can be performed; this will usually be a matter of hours. If the infusion is to be continued for more than seven days, the investigator should contact the monitor.

Progress:

A total of seven patients were entered in this study. Collected data from numerous investigators has demonstrated efficacy and the drug has now been approved by the FDA.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 78/25 Status: Ongoing

Title:

Antibiotic Prophylaxis for Recurrent Otitis Media: Comparison of Sulfasoxizole, Erythromycin, and Placebo

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC M. Weir, MC

Dept/Sec: Pediatrics

Assoc Investigators

Key Words:

Otitis media

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To compare the effect of chronic administration of oral sulfasoxizole, erythromycin or placebo has upon the number of ear infections in children with a history of recurrent otitis media.

Technical Approach:

Children under the age of six years who, upon review of their outpatient chart, have a documented history of four or more ear infections in the preceding twelve months will be considered eligible for the study. Children with previous history of PE tubes, cleft palate or immune disease will be excluded. After informed parental consent, the children will be placed on either sulfasoxizole 25 mgm/kg/dose b.i.d., erythromycin 10 mgm/kg/dose b.i.d., or placebo for a three-month period. During this time the patient will be followed monthly with impedance tympanometry and physical examination. Any new ear infections during this period will be treated with systemic antibiotics for ten days. During the second and third three-month period an alternate drug will be used. Each patient will be followed for nine months and will serve as his, or her, own control. (Three months on Sulfasoxizole, 3 months on placebo, 3 months on erythromycin) in random order. At the conclusion of the study, the frequency of ear infections in children receiving placebo will be compared to those receiving sulfasoxizole or erythromycin.

Progress:

Preliminary data on 20 patients has been analyzed. On erythromycin the incidence of otitis media dropped to 1 in 20 compared to 8 episodes in 11 patients not receiving erythromycin. Incidence based on two month periods was 0.05 and 0.9 respectively. An abstract has been submitted and further patient entry is continuing.

Detail Summary Sheet

Date: 1 Oct 81	Prot No: 80/2	Status: Ongoing
Title: Developmental Analysis of Heavy and Trace Element Hair Content in Normal Children and Children with Attention Disorders		
Start Date:	Est Comp Date:	
Principal Investigator:	Facility:	
LTC P. LoPiccolo, MC		
Dept/Sec: Pediatrics	Assoc Investigators	
Key Words:		
Trace elements		
Accumulative MEDCASE Cost	Est OMA Cost: \$605 (605)	Periodic Review Results
Study Objective:		

To investigate developmental changes in the influence of heavy and trace elements on the behavior of normal children and children with attention disorders.

Technical Approach:

Twenty-five normal children and twenty-five children who have been diagnosed as having an attention disorder with excessive activity will be selected from each of the following age groups: Seven-year olds, nine-year-olds, and eleven-year-olds. An additional group of nine-year-old attentional-disordered children will be selected who are currently on medication. One tablespoon of hair will be collected from the nape of the neck. Ten mm of hair nearest the skin will be trimmed to provide the sample. Information will also be solicited regarding such areas as the date of the most recent hair washing, use of medication, and diagnostic status. Achievement information for the normal children will be acquired using the Wide Range Achievement Test (WRAT), while intelligence scores will be computed using the Peabody Picture Vocabulary Test (PPVT). The hair samples will be stored in plastic bags and coded in a manner so that an individual child's name is not associated with the results. Once the required number of hair samples has been acquired, the samples will be analyzed using atomic absorption spectroscopy. Comparisons of each of the element levels for the normal and attention disordered children will be made in order to identify a possible relationship between the levels of certain elements and the performance of certain intellectual activities.

Progress:

Specimen collection is complete. Analysis has been slowed by malfunctions of the AA spectrometer and electrical mechanical modifications of the facility.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/27 Status: Completed

Title:

Investigation of the Concerns, Perceptions and Expectations of Parents Coming to the Developmental Evaluation Clinic for the First Time

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT E. Krug, MC

Dept/Sec: Pediatrics

Assoc Investigators

Key Words:

Developmental evaluation

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To understand the concerns, perceptions and expectations of parents whose children have developmental problems, when they come to the developmental evaluation program.

Technical Approach:

All parents bringing their children to the DE clinic for the first time (initial workup) will be asked to complete a questionnaire. When 100 questionnaires have been accumulated summary statistics will be analyzed to determine (1) the most common source of referral to the DE Clinic; (2) the most common questions to which parents wanted an answer; (3) the accuracy of parent perceptions about the function and capabilities of the DE Clinic; and (4) the accuracy of parent perceptions of their child's problem. A followup questionnaire will be utilized to determine the correlation between parent perceptions/biases and the degree of ease (or difficulty) with which DE prescriptions are carried out. It may be that compliance with DE suggestions and regimens is related more to parent understanding of the problem than to resistance to the mode of therapy per se. The acquisition of this information may allow us better to meet the needs of our patients and their families in the Developmental Evaluation Clinic.

Progress:

Between May and August 1980 approximately 100 questionnaires were distributed to parents of children entering the Developmental Evaluation Clinic (D.E.C.) at William Beaumont Army Medical Center. The purpose was to examine the concerns of these parents and their perceptions of what the pediatricians in the D.E.C. would be able to

offer. Parents were asked to categorize their child's problem as physical, emotional, a learning problem, a family problem, an inherited problem, and/or a behavior problem. Open-ended questions were asked to elicit parental perceptions and concerns regarding the problem. Finally, the parent was asked to complete a section in which he rated from 1 to 10 (little importance 1-3; moderate importance 4-7; very important 8-10) the value to him of fourteen separate services that might be offered by the D.E.C.

Eighty-nine questionnaires were retrieved for analysis. The following results were of particular interest. First, with regard to the nature of the child's problem, parents felt that in 61% of cases a behavioral and/or emotional and/or family problem was present. A physical component was identified by the parent in 31%, a learning component in 45%, and a genetic component in 7%. Second, when asked specifically about their child's behavior, 18% of respondents noted attention problems, excessive talking, easy frustration with tasks, and overactivity in their child. Third, with respect to Development Clinic services, 84% felt that it was very important for the physician to determine the child's strengths and weaknesses, but only 43% felt that an I.Q. score was very important information. Determining the correct educational program for the child was felt to be very important on 75% of questionnaires. Fourth, with regard to the more traditional areas of pediatric practice, 71% of respondents felt that a complete physical examination was very important, but unexpectedly the figure dropped to 57% for making a specific medical diagnosis. Fifth, when asked specifically about the importance of medications to change your child's behavior, 35% of parents (of children with behavior problems) indicated that medicine was very important, 24% that it was of moderate importance, and 33% felt that it was of little importance, 8% gave no response.

In conclusion, this questionnaire covered a multitude of issues but we were particularly impressed with the fact that 1) 71% of children seen for the first time in the D.E.C. were school-age and usually had school function problems, 2) in a majority of the patients (61%) a psychosocial problem was believed present, indicating that the D.E.C. is a major resource for these problems, 3) characteristics associated with hyperactivity were noted in 18% of children - a significant problem, though frequently not primary, 4) determining the child's strengths and weaknesses and the proper educational program were felt to be the most important tasks of the D.E.C., reflecting a certain sophistication in parental attitude. This study supports an expanding role for the Army Pediatric Developmentalist in the areas of educational programming and behavioral counselling.

AD-A114 731

WILLIAM BEAUMONT ARMY MEDICAL CENTER EL PASO TX
ANNUAL PROGRESS REPORT, FISCAL YEAR 1981.(U)
SEP 81 L L PENNEY

F/G 6/5

UNCLASSIFIED

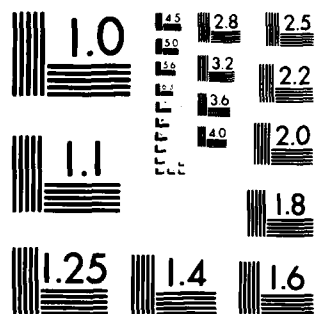
NL

3-13

6-13



END
DATE
FILMED
6 82
DTIC



MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/34 Status: Ongoing
 Title:
 Counterimmunoelectrophoresis in Nonsuppurative Otitis Media

Start Date: Est Comp Date:
 Principal Investigator: Facility:

LTC M. Weir, MC

Dept/Sec: Pediatrics Assoc Investigators
 Key Words:

Otitis media; Counterimmunoelectrophoresis

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost: \$0 (200)	Review Results
Study Objective:		

Test the possibility that antigen persists in middle ear fluid after suppurative becomes nonsuppurative otitis media. It is known that 20-30 percent of middle ear effusions will remain culture positive after the standard course of ten days of antibiotics and even though the fluid on followup examinations has become serous. Further evidence of persistent infection would alter therapy in that initiation or continuation of antibiotics might be indicated. That is, patients who present with serous fluid or develop serous fluid after a standard ten day course of antibiotics may need antibiotic therapy. Twenty to thirty patients will be screened in this pilot study and if persistent infection appears common, a study of extended treatment regimens will be proposed.

Technical Approach:

The usual indications for myringotomy and PE tubes include persistent or recurrent suppurative and nonsuppurative otitis media. The duration criterion for persistence of nonsuppurative otitis media is 2-3 months. This, with or without a conductive hearing loss, is the most common indication for the procedure. Patients are normally referred from Pediatrics to ENT for consideration for the procedure. Patient selection will be by the ENT specialist and not by the primary investigator. When the procedure is performed, the middle ear effusions will be aspirated, the aspirate preserved in a mucus trap, and transported to the laboratory for CIE, culture and gram stain. Aspiration is standard and no additional risk will result from this study.

Progress:

Small numbers of patient volunteers and limited ENT professional support have slowed this protocol. Patient entry continues.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/42 Status: Ongoing

Title:

The Recognition and Frequency of the Polycystic Ovary Syndrome in a General Adolescent Population

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT W.R. LaForce, MC

Dept/Sec: Pediatrics

Assoc Investigators

Key Words:

Polycystic ovary syndrome

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$2825(2825)

Review Results

Study Objective:

To establish the frequency of biochemically proven polycystic ovary syndrome (PCOS) in a general adolescent clinic population, and to evaluate parameters of the medical history in its early recognition.

Technical Approach:

Each year in May through August days are set aside for school and sports physical examinations for dependent children at WBAMC. Approximately 350 adolescent girls are examined on these days. Sera will be collected from approximately 200 of these adolescents after patient and parental consent, and a menstrual history will be obtained. Serologic RIA tests will include the gonadotropins LH and FSH, and the androgen testosterone. Aliquots of serum will be kept frozen for possible subsequent hormone analysis to include estrone, estradiol, androstenedione and insulin. Elevated levels of testosterone, and/or elevated LH, with associated low values of FSH, are biochemical evidence of the polycystic ovary syndrome. Patients characterized as cases of this syndrome will be asked to return to the Adolescent Medicine Clinic for further evaluation, including more comprehensive medical history, and pelvic examination. Those cases identified will be counselled regarding future fertility problems, and offered biochemical regulation of their menstrual periods in an effort to offset the symptoms of this disorder.

Progress:

Samples have been collected from 304 patients. Serum LH, FSH and testosterone will be done on each sample and patients with elevated values will be re-drawn on a standardized day of the menstrual cycle.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/59 Status: Ongoing
 Title: A Longitudinal Prospective Study of the Neurological and Electrophysiologic Development of the Postmature Child

Start Date: Est Comp Date:
 Principal Investigator: Facility:

MAJ Ernest F. Krug, MC

Dept/Sec: Pediatrics Assoc Investigators
 Key Words:

Postmaturity

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

It is currently held that postmaturity may be associated with developmental delays. A recent study of children with developmental delay in language acquisition and electroencephalographic abnormalities in the absence of a seizure disorder has revealed that five out of seven children were postmature. To the best of our knowledge, no serial developmental and electroencephalographic studies have been conducted on postmature children without other pathological conditions up to the present. The purpose of this study would be to fill that gap.

Technical Approach:

A subgroup of postmature children would be identified and included in the study according to standard criteria for postmaturity. The remainder of this group would be infants born at a comparable period postdates but without the usually accepted stigmata of "postmaturity syndrome." These infants would all be compared to a group of normal infants born on or near their due date. Parents would be contacted for informed consent. All participants, control and study, will give the same informed consent. The patient would be studied in a planned longitudinal fashion as follows:

The Brazelton Neonatal Assessment Scale (Brazelton, 1973) would be administered on the 2nd and between the 28th and 30th day of life. A portable EEG would be performed in the Nursery prior to discharge from the hospital and a repeat study carried out at the age of three months and at the age of eighteen months. A neurological exam would

be performed at one year and 18 months. A speech evaluation would be performed at two years and optimally at three years of age. This would be carried out either through a standard evaluation or through a followup questionnaire.

Progress:

Patient accrual is just beginning on this newly activated protocol.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/62 Status: Ongoing
Title: Treatment of Middle Ear Effusions with Oral Hydrocortisone Versus Placebo

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC R.M. Lampe, MC

Dept/Sec: Pediatrics Assoc Investigators
Key Words:
Middle ear effusion; hydrocortisone LTC M.R. Weir, MC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine the efficacy of oral hydrocortisone in the treatment of persistent middle ear effusion in infants and children.

Technical Approach:

Infants and children (six months to 13 years) with persistent middle ear effusion (more than eight weeks) as determined by pneumatic otoscopy and tympanometry, despite systemic antibiotics, and decongestant/antihistamines will be eligible for the study. After informed parental consent, children will be randomly placed (blinded by the Pharmacy Service) on either oral hydrocortisone cypionate 6 mgm/kg/day in three divided doses for the first three days; 4 mgm/kg/day in two divided doses for the next two days; and one dose of 2 mgm/kg/day for one day or placebo (methyl cellulose prepared by the Pharmacy Service) with similar instructions for six days.

Audiometry and tympanometry will be performed prior to treatment and repeated at the one week and two week followup. After two weeks patients who are not cured (normal to improving pneumatic otoscopy and impedance tympanometry) will receive the crossover drug (placebo if hydrocortisone given initially; or hydrocortisone if placebo given initially) and will be followed weekly for two weeks.

Patients with persistent middle ear effusions for three months will be referred for myringotomy and PE tube placement. Patients who are cured will be followed at monthly intervals for six months with pneumatic otoscopy and impedance tympanometry.

The number of patients cleared or failed after initial therapy, crossover, and combined will be compared using chi-square.

	Cleared	Failed	Total
Hydrocortisone			
Placebo			
Total			

Progress:

Six patients have been treated with steroids. No complications have been noted. Patient entry is continuing.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/66 Status: Ongoing
Title: Single Day Therapy with Trimethoprim-Sulfamethoxalate for
Lower Urinary Tract Infection

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC R. Lampe, MC

Dept/Sec: Pediatrics Assoc Investigators
Key Words:

Urinary tract infection

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To determine if a single day of therapy is just as effective as ten days of therapy for lower urinary tract infection. Single day therapy would cut cost, potential development of resistant organisms would be reduced, and patient compliance would be increased.

Technical Approach:

Fifty children, ages 2-12 years will be studied. Children who would not be included: (1) Antibiotic therapy within previous 48 hours. (2) Diabetics. (3) Known anatomic or vascular abnormality of the kidney, or impaired renal function. (4) Any indication of upper urinary tract infection, i.e. flank pain, vomiting, fever greater than 38°C. (5) Known allergy to sulfa drugs.

The diagnosis of lower urinary tract infection will be based upon a) lower abdominal pain, b) frequency of urination, c) urgency or urination, d) dysuria, e) no fever, or fever less than 38°C, no flank pain or tenderness, g) child does not appear ill (toxic).

Laboratory: One or more of the following: a) unspun urine with bacteria but no casts. b) dipstick-nitrite positive. c) greater than 100,000 colonies on two clean catch urines. d) greater than 10,000-50,000 colonies on a catheterized specimen. e) any growth on a suprapubic aspiration of the bladder.

A complete blood count, ESR, and C-reactive protein will be drawn on all subjects in the study. Selection for single day vs. ten day therapy will be random. Fifty envelopes, twenty-five of which will contain the single day protocol, and twenty-five of which will contain the ten-day protocol, will be utilized for the selection.

The subjects of the study will receive 8 mg per kilogram body weight per dose of trimethoprim-sulfamethoxazole. They will receive one dose at the time they are seen in the clinic and one dose at bedtime that same day. The controls will receive 4 mg per killogram body weight per dose of trimethoprim-sulfamethoxazole every twelve hours for a period of ten days.

Each child included in the study will be seen 48 hours after institution of therapy at which time a repeat urine microscopic, dipstick, and culture will be done. At that time children who will be excluded are: (1) initial negative urine culture (2) organism not sensitive to trimethoprim-sulfamethoxazole. (3) Any child who shows signs or symptoms of upper urinary tract infection.

Subsequent to the initial 48 hour followup each patient will be seen two weeks after initiation of therapy, then monthly for six months. All male children will also be studied for urinary tract abnormalities with an intravenous pyelogram and a voiding cystourethrogram.

Progress:

Six patients have entered the study. Failures of treatment appear to be the same in each group. Further patient accrual is continuing.

Detail Summary Sheet

Date: 1 Oct 81	Prot No: 81/37	Status: Ongoing
Title: Torque and Its Relationship to Academic Achievement and Behavior in Children		
Start Date:	Est Comp Date:	
Principal Investigator:	Facility:	
MAJ T.B. Jeffrey, MSC		
Dept/Sec: Psychology Svc	Assoc Investigators	
Key Words: Torque	LTC P. LoPiccolo, MC Mr Thomas D. Carter, Jr, M.Ed	
Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To evaluate the relationship between torque, academic achievement and behavior in children.

Technical Approach:

One hundred children between the ages of 9 and 13 seen in the Pediatric Outpatient Clinic will be evaluated with the following instruments: Torque Test, Wide Range Achievement Test (Jastok, Bijour, and Jastok, 1963), Connor's Abbreviated Teacher Rating Scale, the Burk's Behavior Rating Scale, the Peabody Picture Vocabulary Test, and selected portions of Reitan's Lateral Dominance Examination.

The Peabody Picture Vocabulary Test correlates at a high level (Range = .63 ~ .87) with intelligence scales and requires only a few minutes to administer and score. Groups will be matched (torque versus nontorque) for level of intellectual functioning.

The results of the Torque Test will be scored by employing a single blind procedure. Data will be analyzed dichotomously (torque versus nontorque) to determine if a relationship exists between torque, lateral dominance, academic achievement, and behavior through a multivariate analysis of variance paradigm (2x3x2x2 factorial design). It is hypothesized that those with torque will display mixed lateral dominance on Reitan's test. It is also hypothesized that those with torque will do less well as measured by academic

achievement than their torque-free peers. A third hypothesis is that those with torque will have more behavioral problems as perceived by teachers and parents than their torque-free peers.

Progress:

Patient accrual is just beginning on this newly activated protocol.

Detail Summary Sheet

Date: 1 Oct 81	Prot No: 76/09	Status: Terminated
Title: Development of a Computerized Trauma Registry		
Start Date:	Est Comp Date:	
Principal Investigator:	Facility:	
LTC J.P. Collins, Jr, MC		
Dept/Sec: Surgery	Assoc Investigators	
Key Words: Trauma registry	CPT W.J. Klenke, MSC	
Accumulative MEDCASE	Est	Periodic
Cost \$6,335	OMA Cost: \$0(396)	Review Results
Study Objective:		

To complete development of an automated system for storage, retrieval, and processing of pertinent data for patients with traumatic injury at WBAMC.

Technical Approach:

A computer program will be written to allow the entering, editing, displaying, sorting, classifying and analyzing of patient information. The patients will be restricted to those who are admitted to the Trauma Ward. These records will be used to analyze the epidemiology of traumatic injury and the effectiveness of therapeutic modalities in the management of injured patients.

Progress:

Once again (for the sixth time in the last seven years) WBAMC has a new Chief of the Trauma Service. Data accrual, despite the efforts of the DCI outlined in the FY80 Annual Progress Report, ceased during the Spring of 1981.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 78/03 Status: Ongoing

Title:

National Intraocular Lens Implantation Study

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ Donald J. Bergin, MC

Dept/Sec: Surgery, Ophthalmology

Assoc Investigators

Key Words:

Intraocular lens

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To participate in the study of clinical results of implantations of intraocular lens organized by the Intraocular Lens Manufacturer's Association in response to directives of the Ophthalmic Classification Panel, FDA.

Technical Approach:

An intraocular lens is a prosthetic replacement for the eye's crystalline lens. It is placed in the eye at the time of cataract surgery, where it is fixated by a variety of means, with the intention that it remain permanently and correct the large refractive error remaining after conventional cataract surgery.

Progress:

There have now been a total of 154 implantation operations performed at WBAMC between 22 Nov 77 and 1 Jul 81. There were 11 complications since the last annual review. Two of these were related to accidents which occurred following the patient's hospitalization and the remaining nine consisted of iritis, wound disruption, retinal detachment, lens dislocation, and one patient who required a change of lens size. Except for two of the three patients with retinal detachment, who have limited visual acuity, all of these complications appear to have responded appropriately to therapy. Furthermore, all of the complications are those which would be anticipated with this type of operative procedure, whether the intraocular lens was being utilized or not.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 79/43 Status: Terminated

Title:

Perioperative Thrombosis Prophylaxis in Patients with Peripheral Vascular Disease

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC J.T. Collins, MC

Dept/Sec: Surgery, Trauma Ctr

Assoc Investigators

Key Words:

Thrombophlebitis

Accumulative MEDCASE

Est

Periodic

Cost \$4,000

OMA Cost: \$3,000(3000)

Review Results

Study Objective:

To determine the efficacy and safety of low-dose heparin prophylaxis in patients undergoing peripheral vascular surgery.

Technical Approach:

Patients entering the hospital for a proximal revascularization (aorto-iliac bypass, aorto-iliac endarterectomy, aorto-femoral bypass) procedure will be randomly assigned to either a control or a treatment group. Patients in the control group will receive no thrombosis prophylaxis. Patients in the treatment group will receive 500 u of heparin subcutaneously each 12 hours for ten days after the methods of Kakkar and co-workers, and Flanc and co-workers. Heparin given intraoperatively will be reversed in keeping with out usual practice.

Venous thrombosis will be demonstrated using the 125I-fibrinogen leg scans. 125I-fibrinogen is converted to fibrin under the influence of thrombin, thus incorporating 125I into a developing clot.

Commercially available 125I-fibrinogen is a derivative of single-donor human plasma. These donors are carefully screened for blood borne, transmissible diseases, particularly hepatitis. No cases of hepatitis or other illnesses have been reported with the product to be used.

To perform test, the freeze dried preparation is reconstituted with sterile water at the time of injection. A routine 1 cc dose

consists of 2 mgm of clottable protein, and 140 mCi of ^{125}I . All patients will receive 250 mg (5 drops) of saturated KI orally 24-hours prior to injection of ^{125}I -fibrinogen to effect thyroid blockade.

^{125}I decays by electron capture with a physical half-life of 60 days. There is no beta emission. Photons are of x-ray (35 KEV) and K x-ray (28 KEV).

External radiation is 1.5/mc/hr at 1 cm. Radiation dosimetry is as follows: thyroid (unblocked), 1.3 R/100 ci; thyroid (blocked), 0.02 R/100 Ci; whole body, 0.02 R/100 Ci.

The administration of ^{125}I -fibrinogen and scintillation counting for each patient will be performed by the Nuclear Medicine Service, WBAMC under the direction of LTC H.W. Henry, MC. The thrombus detector, to be purchased by the Dept Clinical Investigation, utilizes a thallium activated sodium iodide crystal. Counts will be taken daily beginning 24-hours after injection of the isotope and for a period of ten days unless an abnormal scan is noted. Therefore, the first dose will be given two days before the operation.

The scanning procedure consists of passing the above described hand held device over the patients' sternum and at various levels of both lower extremities for periods of five to thirty seconds. Abnormal concentrations of ^{125}I in the lower extremities correlate well with deep venous thrombosis. The counting device is easily transported, the exam is quick and noninjurious to the patient, and it will be performed at the patients' bedside. ^{125}I -fibrinogen leg scanning is now a well-accepted procedure in many hospitals.

Accurate documentation of all other thrombotic events will also be sought. Cerebrovascular accident will be diagnosed clinically and confirmation will be sought by vascular and static brain scans. Suspected myocardial infarction will be confirmed by electrocardiogram and serial cardiac enzyme determinations. Patients who develop a positive ^{125}I -fibrinogen scan will have a phleborheogram performed daily. If the phleborheogram is positive, the case will be judged a failure of prophylaxis, and heparin will be begun by continuous infusion with the goal of keeping the activated partial thromboplastin time at 1.5 to 2.5 times normal. Phleboheography as developed by Cranley and co-workers has been confirmed by us to be 95.3 percent accurate for detecting clinically significant venous thrombi. Phleborheography is a noninvasive test with no risks to the patient. Suspected pulmonary embolism will be confirmed by chest x-ray, arterial blood gases, pulmonary scans, and pulmonary arteriography when indicated.

All patients will be counselled regarding the various ramifications of the protocol and will sign a human volunteer agreement prior to entry into the study. It is estimated that 100 patients will be entered into the protocol over a two-year period. Data concerning the perioperative management will be available at the end of two years. In the unlikely event that a patient with a contraindication or allergy to heparin should be considered for operation, he will be excluded from the study. Female patients, aged 15 to 50 years, will be screened with pregnancy tests and positive results will serve as a basis for elimination from this protocol.

Should a hemorrhagic complication develop, heparin administration will be discontinued. Although ecchymoses may develop at the site of heparin injection, the chance of developing wound hematomas or life threatening hemorrhage from low-dose heparin, properly administered, is essentially nil. A thrombin time will be obtained and circulating heparin will be neutralized by protamine if necessary. We will attempt to correlate the eventual outcome with the preoperative profiles.

Progress:

The principal investigator discontinued this study prior to his resignation in early calendar year 1981.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/12 Status: Ongoing

Title:
Effect of Systemic Anti-Neoplastic Chemotherapy on Dacron Graft Incorporation

Start Date: Est Comp Date:

Principal Investigator: Facility:

CPT J.R. Daniel, MC

Dept/Sec: Assoc Investigators

Key Words:
Thoracoabdominal aortic graft; LTC J.T. Collins, MC
Platelet survival time LTC T.J. Brown, DO
David O. Rauls, PhD

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost: \$11,305(13,829)	Review Results

Study Objective:

To determine the effect of systemic cancer chemotherapy on the healing events which allow incorporation and formation of a neointima in dacron prosthetic grafts.

Technical Approach:

Graft incorporation will be followed by platelet survival times. This is an accepted measure of graft incorporation with platelet survival being reduced by fifty percent immediately after graft placement and returning to normal as the graft is incorporated. Also dogs will be sacrificed at six weeks and six months for histological examination of graft healing. Any dogs which die or develop complications related to the graft will be histologically studied. Graft incorporation will be studied in the following settings: (1) A graft placed simultaneously with initiation of chemotherapy. (2) A graft placement after initiation of chemotherapy. Three controls will be used. In one group platelet survival will be followed without any treatment, to monitor consistency of technique of platelet survival determination. In another group platelet survival will be monitored before and during chemotherapy. A third group will have a thoracoabdominal graft placed without chemotherapy.

Progress:

Publications and presentations to date from this study have been listed in the tables in this and previous Annual Progress Reports. A current manuscript in preparation outlines further progress:

Adult beagle dogs of both sexes were used. Forty-two milliliters of blood were withdrawn from the jugular vein into a 50 ml plastic syringe containing 8 ml of acid citrate dextrose, modified (Squibb A-C-D, modified). The blood was transferred to a 50 ml sterile plastic centrifuge tube and centrifuged at 180 g for 5 min to remove excess red cells. The platelet-rich plasma was transferred to another centrifuge tube, made 5 percent with respect to acid citrate dextrose (modified) and centrifuged at 800 g for 15 min to give a platelet pellet. The pellet was gently washed with 3 ml of isotonic saline solution, then suspended in 3 ml of saline for labeling. About 100 μ Ci of indium-111 oxine (Medi-Physics, Inc., Emeryville, CA) in about 0.05 ml of ethanol was added to the platelet suspension. The suspension was mixed gently at room temperature for 15 min and centrifuged at 800 g for 15 min to give a labeled platelet pellet. The pellet was washed with 3 ml of autologous platelet poor plasma then resuspended in 3 ml of platelet poor plasma. The suspension was withdrawn into a 5 ml plastic syringe and injected into a cephalic vein followed by a saline flush. Total time required was less than three hours with the maximum time in saline 0.5 hr.

Blood samples were withdrawn into a plastic syringe and transferred to a plastic tube containing 0.2 ml of dipotassium (EDTA) (10). Duplicate 2 ml aliquots were pipetted into counting tubes containing 1 ml of water to promote cell lysis. Samples were collected at 0.5, 2 and at 24-hour intervals with the last sample taken at 96 hours post-injection. The samples were counted in a Beckmann 4000 gamma counter optimized for counting indium-111.

Figure 1 gives frequency distributions for mean platelet survival times calculated according to each of four models. With the exception of the weighted mean, all of the models give frequency distributions approximating a normal distribution. Use of the weighted mean apparently gives rise to increased calculation error as indicated by the broad distribution of values. It should be noted that the formula for the weighted mean of the International Committee for Standardization in Hematology gives values heavily weighted toward the linear value and different from the value for the weighted mean obtained from the computer program provided by the authors.

Figure 2 is a composite of the data from 47 animals and illustrates the typical shape of the disappearance curves. There was no early rapid clearance of platelets indicative of platelet damage. The mean value for 47 dogs (linear model, 129.7 ± 12.8 hrs) was in good agreement with that found for six dogs by Lotter et al. (124.5 ± 10.5 hrs) whose labeling technique was followed.

Mean platelet survival times for a group of five dogs were followed over a period of six months. While there was considerable animal-to-animal variation, values for individual animals remained fairly constant except for early in the study when technique was being developed (Fig 3).

DISCUSSION

A number of researchers have reported mean platelet survival times in dogs. Most have used the linear model in reporting their results. The model used for calculation affects not only the absolute value of the mean platelet survival time, but also the frequency distribution of the values. The use of the weighted mean gives an unacceptably broad range of values.

The component of the overall error introduced by inadequacy of the mathematical model chosen can be decreased by choice of the appropriate model. Murphy et al. have provided a strong argument for use of the multi-hit model. The linear model gives reproducible values in normal animals where the disappearance curve is unaffected by pathological conditions causing a rapid clearance of platelets resulting in a decidedly nonlinear curve. However, platelet survival data is often obtained for the purpose of detecting and defining pathological conditions and the model used should be that which best fits nonlinear data.

Mean survival times reported for canine platelets calculated by the linear method range from a low of 124.6 hrs to a high of 192 hrs (Table 1). One source of the wide range of literature values is the use of the linear model for calculation of the survival time. The value obtained is strongly affected by any initial rapid platelet clearance as well as by the number of data points collected on the tail of the disappearance curve. Another reason for the wide range of values found in the literature is the variety of labeling techniques used. Lower values obtained from platelets labeled in isotonic saline have been attributed to loss of platelet function or damage to the cell while in isotonic saline. Others have reported that isotonic saline was acceptable as a labeling medium for canine platelets, but not for human platelets.

We report data obtained from 47 animals over an 18-month span using isotonic saline as the labeling medium. These values have a standard deviation comparable to that reported by other laboratories using a variety of labeling techniques (Tables 1 and 2). The variation observed is due to a combination of biological variation and experimental error. Table 2 summarizes the important statistical data from these 47 dogs as calculated by each of the four survival models.

While the data presented here from platelets labeled in isotonic saline give a lower mean value relative to literature values (linear model) for platelets labeled in plasma, the statistical distribution of the data is not highly skewed to lower values as would be expected for inclusion of low values resulting from damaged platelets (Fig 1). The shape of the disappearance curve (Fig 2) is comparable to that reported by other workers and does not reflect an early rapid clearance indicative of damaged platelets.

Data collected from a group of five dogs, whose platelet survival times were followed over a period of six months, illustrate the technique dependence of labeling procedures. Platelet survival times were measured over a period of six months at widely spaced intervals after the initial determination. Note that data from four of the five animals were very reproducible over a period of time, even though results were quite variable from animal to animal (Fig 3). Early variability in the data relative to the results of the last three determinations indicates that experience in the technique is important in order to obtain reproducible results. Data from one animal showed a definite trend downward, followed by partial recovery. It is possible that this animal had health problems affecting platelet kinetics that went undetected by the veterinary personnel.

The results reported here indicate that reproducible measurements of canine platelet survival times can be accomplished over an extended period of time using isotonic saline as the labeling medium. However, the method is technique dependent and care must be taken to minimize the contact time with the saline. Also, close attention must be paid to sampling and calculation procedures. Our results support the multi-hit model developed by Murphy et al. as an adequate model for calculating platelet survival in those cases where nonlinear curves may be anticipated. If ease of computation is a factor, the experimental model is adequate.

LEGENDS:

FIG 1:

Histograms of platelet survival data calculated by different mathematical models. A) linear, B) exponential, C), multi-hit, and D) weighted mean. Coefficient of skewness: A) 0.494, B) 0.079, C) 0.582, D) 0.383.

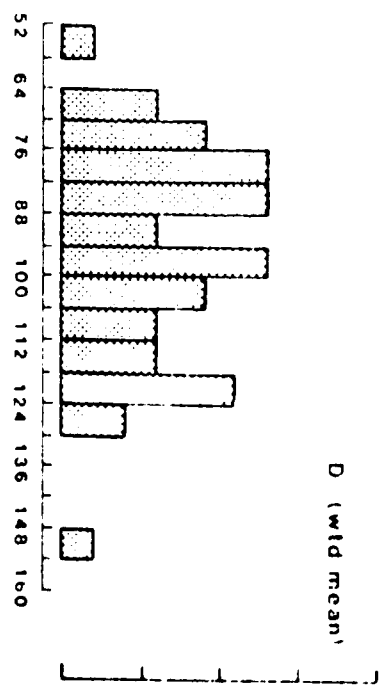
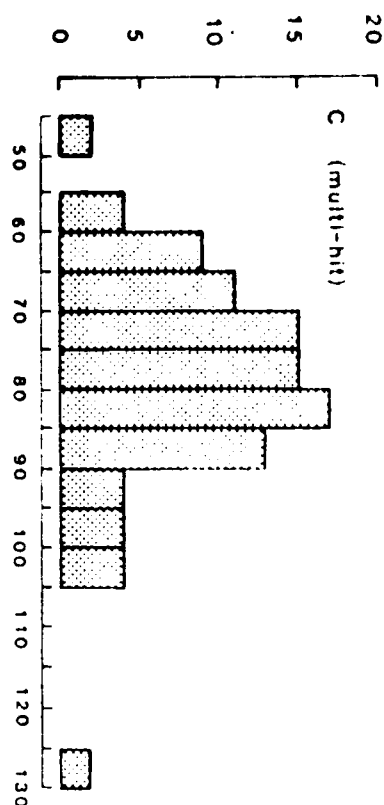
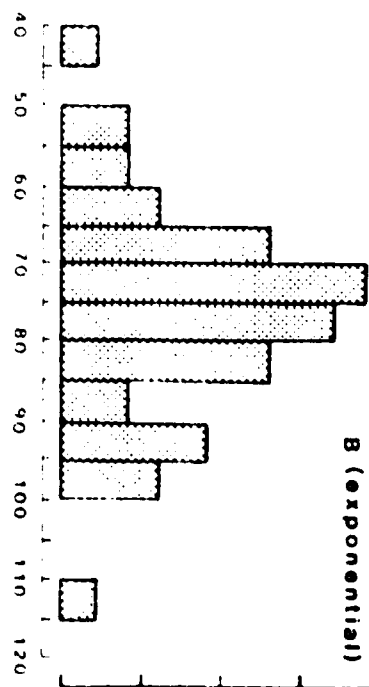
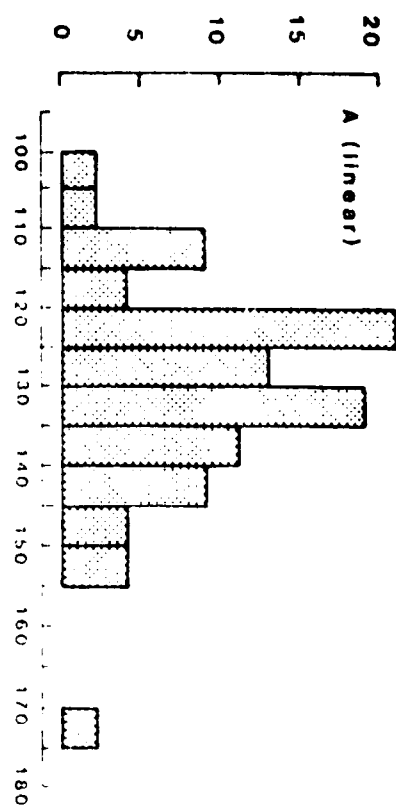
FIG 2:

Mean platelet survival curve for dogs. Each point a mean of 4/ determinations.

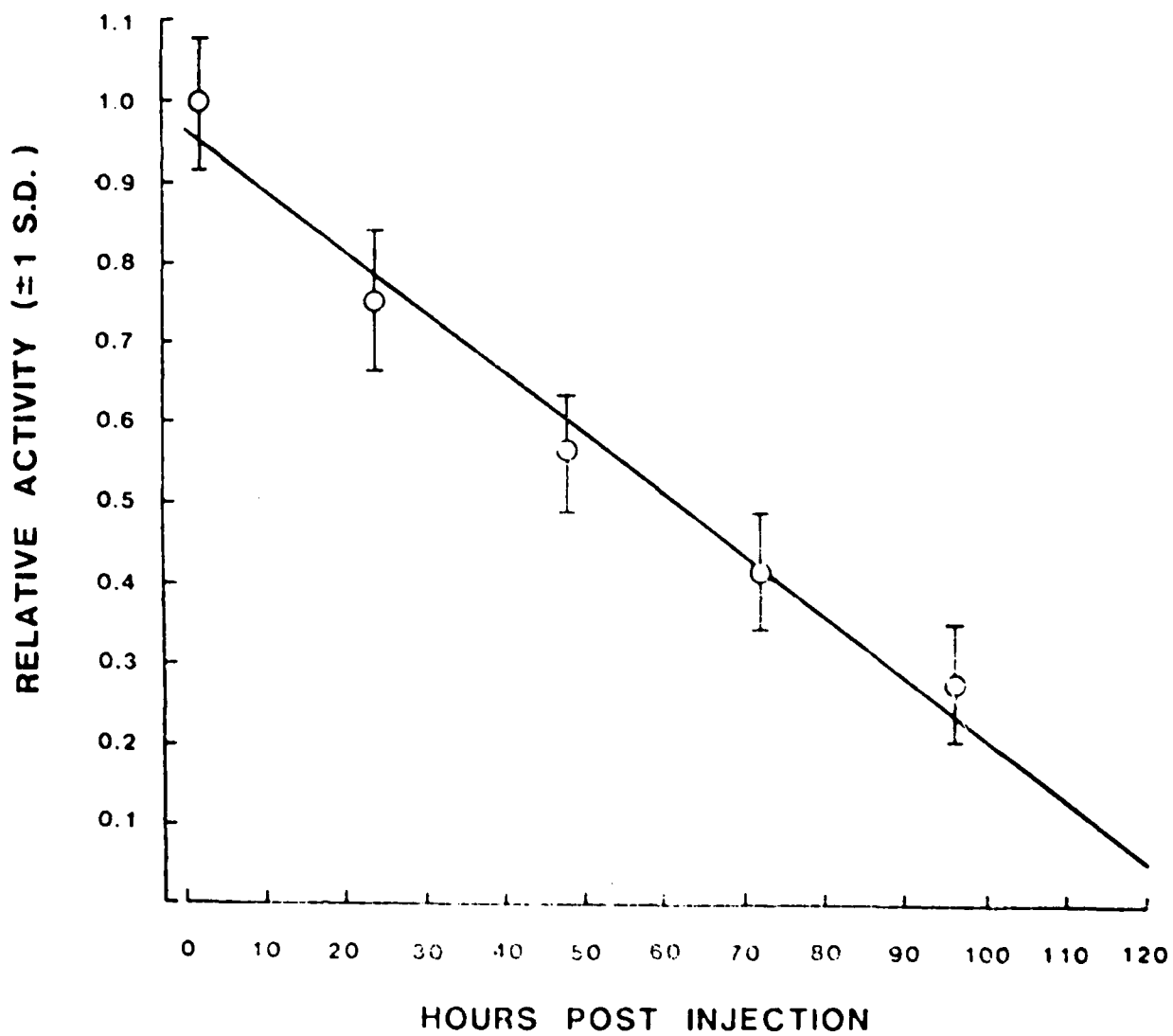
FIG 3:

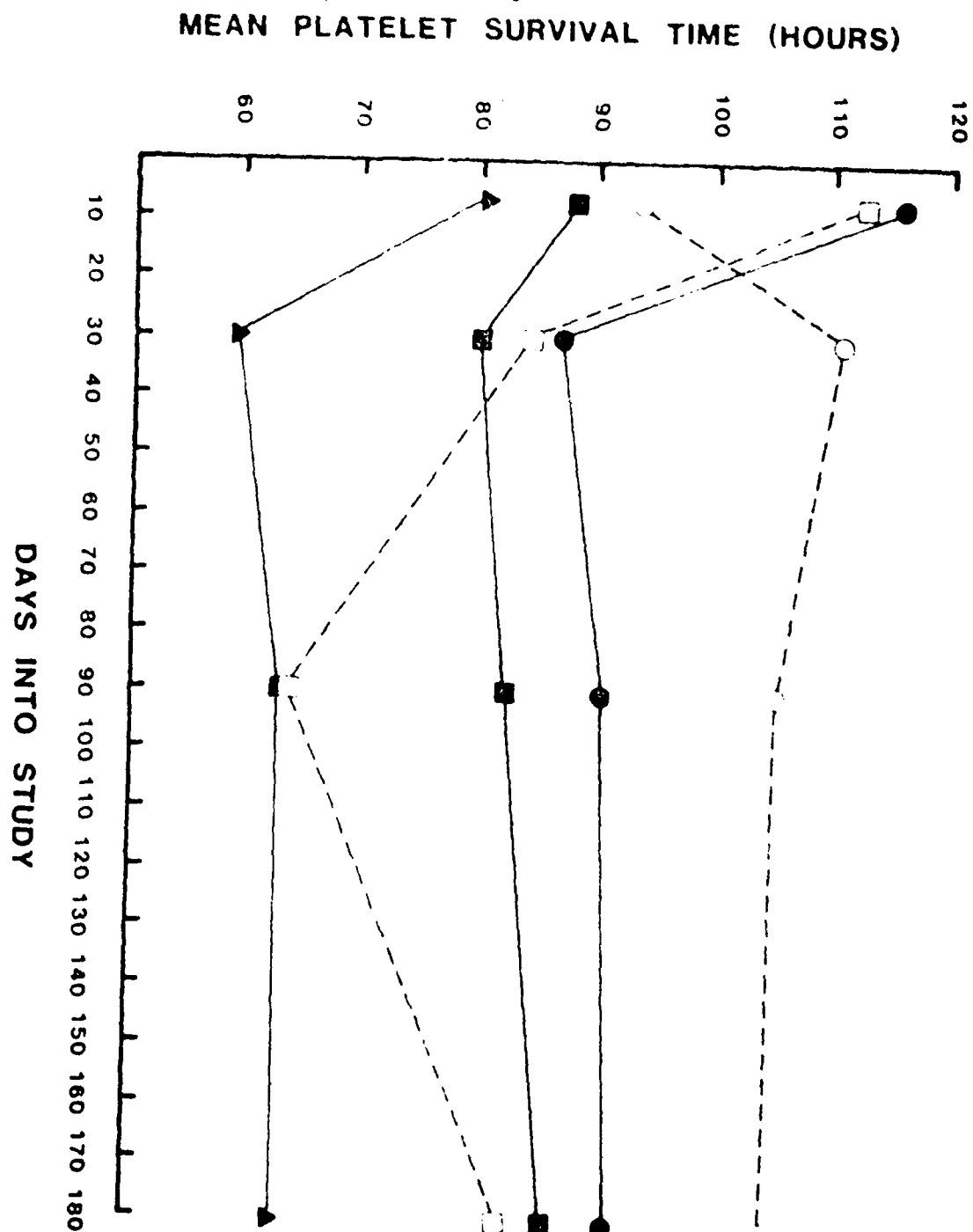
Reproducibility of platelet survival times for five dogs followed over a six-month period. Mean platelet survival times calculated by multi-hit model.

PERCENT RELATIVE FREQUENC



MEAN PLATELET SURVIVAL TIME (HOURS)





Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/30 Status: Terminated

Title:

Physiologic Monitoring and the Manipulation in the Aortic Reconstruction Patient

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC J. Collins, MC

Dept/Sec: Surgery

Assoc Investigators

Key Words:

Aortic reconstruction

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To assess the effects of shock trousers at varying degrees of compression upon the cardiovascular system and patients about to undergo aortic reconstruction, to optimize patient's cardiovascular status in terms of left ventricular stroke work index, peripheral vascular resistance, and cardiac index prior to undergoing major aortic reconstruction and to assess the benefits of this approach in the intra- and postoperative period.

Technical Approach:

All patients scheduled for elective aortic reconstruction on the day prior to surgery are admitted to the Trauma Unit or Surgical Intensive Care Unit where Swan-Ganz balloon catheters and arterial lines are placed. Following placement and the baseline determination of multiple parameters outlined in the protocol, shock trousers are placed and varying degrees of compression applied. At each level of compression these parameters are remeasured. Following this, the trousers are removed and varying amounts of lactated Ringers solution is administered intravenously and the effects of intravenous infusion on the cardiovascular parameters are determined. Following achievement of "optimum" cardiovascular parameters, the patient is considered prepared for surgery and subsequently undergoes the scheduled aortic reconstructive procedure.

Progress:

None. The principal investigator has resigned.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 80/42 Status: Terminated

Title:

Pilot Study for the Use of the Automated Autologous Blood Recovery System (Cell Saver) in Blunt and Penetrating Abdominal Trauma

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC J.T. Collins, MC

Dept/Sec: Surgery

Assoc Investigators

Key Words:

Cell saver

CPT J.A. Camunas, MC
CPT T.E. Gaines, MC
COL A. Kissack, MC

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To establish the effectiveness of the automated autologous blood recovery system (cell saver) in providing an economical, efficient, safe source of autologous red blood cells for patients undergoing elective surgical procedures and in decontaminating free peritoneal blood associated with blunt and penetrating thoracic and abdominal trauma.

Technical Approach:

The automated autologous blood recovery system will be used in trauma patients presenting with either blunt or penetrating abdominal or chest trauma. In addition, all patients undergoing elective thoracic, gastrointestinal, and vascular surgical procedures in which significant attendant blood loss is anticipated will be included in this study. Intraoperatively, aerobic and anerobic blood cultures and gram stains of the free intrathoracic and peritoneal blood will be obtained. The autologous blood recovery system will be used in recovering this free blood. After the blood has been collected, washed, and packed by the cell saver system, anerobic aerobic cultures will be obtained as well as white blood cell count, red blood cell count, platelet count, Wright stain, plasma-free hemoglobin, heparin, fibrinogen and gentamycin levels. This will be done on all collections by the cell saver. In cases where contamination of the blood by enteric contents is

documented, the washed, packed red blood cells recovered will not be given to the patient. Postoperatively the patients who have received noncontaminated and washed red blood cells will be followed closely for clinical signs of sepsis. When indicated serial blood cultures will be obtained and the patient treated with appropriate antibiotics pending culture results. The wash solution used during the recovery system will contain 80 mg of Gentamycin per liter of wash solution. This has been demonstrated to effectively eliminate aerobic organisms from the washed cell product as well as pathogenic anerobic organisms. Also it has been demonstrated that the cell saver effectively removes essentially all free gentamycin from the red cell product.

Progress:

None. The principal investigator has resigned.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/02 Status: Ongoing

Title:

Replacement of the Infra-Renal Inferior Vena Cava with an Improved Expanded Polyfluorotetraethylene (e-PTFE) Graft and Comparison of Two Graft

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT T.E. Gaines, MC

Dept/Sec: Surgery

Assoc Investigators

Key Words:

Vena cava; PTFE vascular grafts

LTC J.T. Collins, MC

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To evaluate an improved e-PTFA(IMRA) graft in the infra-renal vena cava in dogs. Parameters studied will be those of initial pressure, flow characteristics, and patency. Histologic appearance will also be studied should thrombosis or occlusion occur. The effect of graft diameter is to be compared for two graft sizes, one smaller than, and one approximating, the diameter of the native vessel. Our goal is to work toward developoiment of the reliable grafting procedure and prosthetic material for replacing important veins in humans.

Technical Approach:

Dogs will be used as the animal model. It is intended to use the optimum synthetic material and grafting procedure in this study and to test the material and procedure in the most difficult situation. Therefore, an A-V fistula will be employed and anticoagulation will be considered at the time of the procedure. The hemodynamic effect of the A-V fistula will be monitored with blood flow and pressure studies. The graft material will be e-PTFE which has a pore size of approximately 30 microns. The graft will have rigid external support consisting of a spiral of solid teflon. The length of the graft will be 6 cm so as to provide a length that has clinical utility. In addition to the above considerations the effect of velocity of flow will be studied with this experiment. Two graft sizes will be used, one being 8 mm and approximating the native size of the inferior vena cava in the dog, the other, 5 mm, being narrower. Presumably flow does not decrease through the narrower

graft (an assumption to be measured in the study). The velocity of flow would be higher than through the larger graft. The effect of this higher velocity of flow may be to improve patency and this will be monitored.

Progress:

This study will be activated as soon as adequate animal space in the Biological Research Facility is available.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/07 Status: Ongoing

Title:

Comparison of Mortality and Morbidity of Uretero-
ileocecosigmoidostomy With Other Urinary Diversions.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL F.L. Diaz-Ball, MC

Dept/Sec: Surgery

Assoc Investigators

Key Words:

Ureteroileocecosigmoidostomy

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

At present, the urinary diversion methods accepted as effective have been the ones which require an external appliance over a stoma and on occasion ureterosigmoidostomy. Examples among these are: The ileal loop or conduit of Bricker, ileocecal loop, or the colonic loop. All these are prone to complications and are less ideal. In 1972 the senior investigator and associates reported on a study in dogs done at Letterman Army Medical Center in which the feasibility of an internal diversion using a uretero-ileocecosigmoidostomy was established. The anti-reflux action of the ileo-cecal valve can be enhanced with the newly developed Zinman technique. Prior to a wide application in humans, we should prove that the incidence of complications is comparable or preferably less than the accepted methods used at this time. It is projected to perform surgery in control groups of ileal loops, colonic loops, ureterosigmoidostomies and compare incidence of complication with equal numbers of uretero-ileo-cecosigmoidostomies.

Technical Approach:

1. Control Group I - a series of 6-12 dogs will undergo ileal loop diversion.
2. Control Group II - a series of 6-12 dogs will undergo a colonic loop.
3. Control Group III - a series of 6-12 dogs will undergo a ureterosigmoidostomy.

4. Tested Group IV - a series of 6-12 dogs will undergo uretero-ileocecosigmoidostomies.

Data Collection:

Preoperative: Will include serum creatinine, BUN, and CBC. Urine C and S if possible, IVP and R.C. Barium enemas would be performed to establish functional integrity of urinary and bowel tracts including ileocecal valve competence. Kidney biopsy for regular and electron microscopy. **Intra-operative:** serum creatinine, BUN, urine from renal pelvis or ureters for C and S, urine aspirates from bladder for C and S.

Postoperative: Every 1-2 weeks BUN and creatine. Every month an IVP, and every 2 months a cystogram. Will be as in humans with IVs until safe to feed, etc. At least every 1-2 weeks repeat CBC, BUN, creatinine, retrograde cystogram every month times 3 and then every 3 months times 3.

Long Term: Dogs will be kept ideally at least one year alive, facilities permitting. At that time they could be sacrificed, autopsied for detection of changes due to surgery in the urinary system and other systems.

Control groups I and III, and the test group will comprise the initial study. If time and funding permit, control group II, and possibly another group with ileo-cecal cutaneous diversion, may be compared to the tested group.

Progress:

This study will be activated as soon as adequate animal space in the Biological Research Facility is available.

Detail Summary Sheet

Date: 1 Oct 81 Prot No: 81/49 Status: Terminated

Title:

A Comparison of Techniques for Obtaining Tissue for Estrogen Receptor Analysis in Human Breast Cancer

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT W.J. Todhunter, MC

Dept/Sec: Surgery

Assoc Investigators

Key Words:

Estrogen receptor

MAJ M.A. Piskun, MC

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To compare the value of tissue obtained at breast biopsy with tissue obtained from a mastectomy specimen for estrogen receptor analysis.

Technical Approach:

A study is proposed in which 30 breast cancers will be studied. In each case the tumor will be biopsied and a specimen sent immediately for estrogen receptor assay. This will be done either in the General Surgery Clinic or in the operating room immediately prior to mastectomy. A second specimen will be taken from the mastectomy specimen immediately after removal of the entire specimen from the body. This will also be sent for estrogen receptor assays then will be compared to determine if there is a difference in the results.

Progress:

Data from similar experiments were done elsewhere and published prior to activation of this protocol. This data precluded proceeding with this study.

INDEX

INVESTIGATORS

Anees M 71
 Artalejo L 20
 Aspinall K 20
 Aubin BA 147
 Baker FJ 141
 Baker MJ 180
 Benedetto AR 15
 Bergin DJ 204
 Betz G 15
 Billingsley JL 16
 Bohman D 101
 Bonnell JR 146
 Boyce D 158
 Boyd DB 49
 Brown JM 16
 Brown TJ 17, 54, 76, 86, 109
 Burg K 21
 Butler A 20, 21
 Cavanaugh DG 21
 Cerezo L 19
 Chaffin J 20
 Collins JP 203, 205, 222, 223
 Copeland R 18, 21
 Cotterill RW 171, 173
 Couvillion CE 22
 Covarrubias GA 18
 Dahlander RC 149
 Daniel, JR 208
 Daniell WC 15, 18, 155, 157, 159, 163, 166
 Daniels DL 16
 DeFiore RJ 19, 20
 Diaz-Ball FL 227
 Duarte CG 17
 Engel T 15
 Fariss BL 15
 Farley PC 61-65, 67-69, 72, 78-81, 84, 87, 89-93, 96, 114-122
 Floyd JL 17
 Frederick RJ 15, 30, 32, 33
 Friedman HL 19
 Gaines TE 225
 Gamez A 20
 Gauld JR 21
 Geer TM 21
 Gluhm DP 51
 Gouge SF 145
 Graham G 97
 Greenberg H 21, 169
 Heath RE 20
 Henry HW 16, 56

Herrera GA	19,20
Hoadley S	16
Hopkins CD	19
Howard TE	18
Huntt HA	19
Jacob WH	15
Jeffrey TB	201
Kaufman MF	20
Killam AP	15,18
Klenke WJ	15
Krug E	191,195
LaForce W	21,194
Lampe RM	20,21,197,199
Latham RD	102,113
Levey IL	136
Livaudais W	21
LoPiccolo PF	186,189
Lorenzen E	21
Lull RJ	16
Lundy MM	16
Maccario M	16,138,140
Mansfield LE	16,58,70,75,82-85,88,89,105,107,111,124,126,127,129,131,133,134
Mateo LA	15
McAuley RJ	16
McLeod H	20
Mead JH,	20
Mendoza A	19
Miles PA	15
Moreno AL	17
Morrison RE	17,21,53
Nelson HS	16
Nusynowitz ML	17
Old C	17
Parker AL	17
Parker G	18
Patterson S	21
Pearl W	187
Penney LL	15,18,36,42,43,44,164,185
Pesetski JD	18
Pitcher JL	17
Plymate SR	15
Ramirez G	21
Rauls D	15,17,18,35,45,168,170
Reamy K	18
Redwine MD	16
Reimann BEF	18,19,20,156,184
Richey HM	60

Rogers JA	20
Ruangwit UI	15
Ruggles JE	46
Rychly R	17
Schwab J	21
Schydlower M	21
Scully TJ	19,20
Sellers, M	55
Shervette R	21
Siedlecki M	17,74,123
Silsby HD	21
Simonson DC	151
Smith ML	15,37,38,39,41
Smith S	94
Smith WR	19,182
Sonnemaker RE	17
Spicer MG	17
Stafford JO	18
Stein MR	17
Sullivan E	153
Swaney J	21
Thompson DA	18
Ting S	17
Todhunter W	229
Turnbull GL	17
Vaughn DL	174
Vichick DA	19,176,177
Weir MR	20,21,188,193
Weissman J	128
White SE	18
Youkey JR	21
Zwolensky JR	50

INDEX

SUBJECT

2,3-diphosphoglycerate	55
Actinomycin D	164
Acute renal failure	74
Adrenal scanning	54
Alcoholism	71,84
Alveolitis	50
Amniotic fluid	158,163
Antimicrobial agents	30,35,50
Anxiety	149
Aortic Insufficiency	58
Aortic grafts	45
Aortic reconstruction	222
Asthma	94,129,131
Atopy	70
Atrioventricular node	113
Atropine	129
Back Pain	151
Bacterial growth inhibition	158
Beta II agonists	88,107,133
Bone scanning	97
Bronchial hyperactivity	75
Bronchitis	60
Bronchoconstriction	134
Carcinoma, breast	63,79,93,122
Carcinoma, gastric	67
Carcinoma, head and neck	89,90
Carcinoma, larynx	118
Carcinoma, lung	81,87,120,121
Carcinoma, ovarian	115
Carcinoma, pharynx	118
Carcinoma, testis	114
Cell Membrane	33
Cell saver	223
Cerebral ischemia	138
Cesarean section	166
Chemotaxis	124
Chorioamnion	156
Cromolyn	75
Cimetidine	42,127
Coccidiomycosis	128
Colchicine	119
Cortisol	36,42
Counterimmunoelectrophoresis	193
Cyllohexamide	42
Cystography	86
Delayed hypersensitivity	143
Deoxyribonucleic acid	33
Developmental evaluation	191
Diabetes Mellitus	146

Diarrhea	101
Dihydroprogesterone	170
Diphenylhydantoin	186
Ductus arteriosus	187
Electromyography	182
Electrophoresis	136
Embolization	176
Enzyme-linked immunoassay	82,83
Eosinophil migration	133
Erythromycin	124
Estriol	36,164,169
Estrogen Receptors	44,229
Estrone	169
Follicle-stimulating hormone	41
Food allergy	99
Furosemide	145
General anesthesia	49
Glioma	64,92
Glucocorticoids	50
Glucose	49
Gonad	78,91,96
Hemodialysis	123
Hemolysis	153
Hepatitis	71
Hepatobiliary scanning	56,109
Histamine	133
Hodgkin's disease	140
Human chorionic gonadotropin	41
Hyaluronidase	102
Hydrocortisone	197
Hyposensitization	111
Immunization	32
Immunocytochemistry	41
Immunoglobulins	83,88,107
Immunotherapy	85
Intraocular lens	204
Ketoconazole	128
Knee	182
Latex agglutination inhibition	82
Leukemia	69,116,117,119
Lipoxygenase	126
Lupus erythematosus	127
Luteinizing hormone	41
Lymphocyte stimulation	126

Lymphoma	61,65,78,91,96
Mannitol	74
Mast cells	133
Melanoma	62
Middle ear effusion	197
Migraine Headache	99
Molar extractions	50
Molecular etching	181
Multiple myeloma	80
Myocardial infarction	102
Neointima	45
Nephelometry	82
Nifedipine	102
Oleic Acid	176
Orthognathic surgery	46
Osteomyelitis	97
Otitis media	188,193
Ova	78
Oxytocin	36
PTFE vascular grafts	225
Penicillin	46,70
Pericarditis	140
Phenolamine	42
Phosphatidylglycerol	163
Platelet survival time	208
Pneumonia	60
Polyamines	38
Polycystic ovary syndrome	194
Postmaturity	195
Pre-eclampsia	170
Premature labor	157
Prolactin	39,41
Prophylactic antibiotics	166
Prostacyclin	45
Prostaglandin E ₁	187
Prostaglandins	156,159
Radiographic contrast	74
Radioimmuno assay	82
Radiotherapy	140
Renal failure	145
Renal scanning	76
Rheumatoid arthritis	126
Russian Thistle antigen	111
Salicylates	131
Seminal fluid	39
Shikimate	35
Sickle Cell trait	72
Sinoatrial node	113
Skin Grafts	51

Spermatogenesis	37
Spermatozoa	39,91,96
Sputum	60
Streptococci	30,32,141
Streptodornase	143
Streptokinase	102,113,143
Subarachnoid block	147
Surface active phospholipids	168,173
Terbutaline	157,168,173
Tetracycline	53
Thoracoabdominal aortic graft	208
Thrombophlebitis	205
Thyroid hormones	71
Thyroid function tests	55
Ticlopidine	138
Torque	201
Trace elements	171,185,189
Trauma registry	203
Trauma, hand	180
Umbilical Cord Blood	155
Upper Respiratory Infection	53
Ureteroileocecosigmoidostomy	227
Urinary tract infection	199
Uterine blood flow	42,43,159,164
Vena cava	225
Verapamil	174
Vesicoureteral reflux	86
Zinc	185
¹³¹ Iodine	37
17-B-Estradiol	42,43,44

DISTRIBUTION LIST

5 Copies	HQDA(SGRD-HR WASH DC 20310
12 Copies	Defense Documentation Center (DDC) ATTN: DDC-TCA Cameron Station Alexandria, Virginia 22314
1 Copy	Superintendent Academy of Health Sciences, US Army ATTN: AHS-COM Fort Sam Houston, TX 78234
2 Copies	Commander Health Services Command Ft Sam Houston, TX 78234

DATE
FILME
—8